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Vol. 95 JUNE, 1923 No. 6

CONTENTS

Editorial:
"Consider the Lilies" 325

Selected Editorial:
Has Science Reached Its Limit? By Dr. E. E. Slosson 327

Original Articles:
Animal-Eating Plants. (Illustrated.) By Heber W. Youngken, Ph. M., Ph. D., Philadelphia 329
Explosives and Explosions. By Henry Leffmann, Ph. M., M. D., Philadelphia 351
Preparation and Publication of Research Papers. By Arthur W. Dox, Detroit, Mich. 357
The First Half of the First Century of the Philadelphia College of Pharmacy and Science. By Prof. John Uri Lloyd, Cincinnati, Ohio 362

Abstracted and Reprinted Articles:
The Status of Insulin. From the *Journal of the American Medical Association* 369

Scientific and Technical Abstracts 380

Medical and Pharmaceutical Notes 386

Solid Extracts 388

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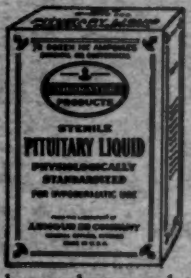

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PHARMACEUTICAL PRODUCTS

THE AMERICAN
JOURNAL OF PHARMACY

VOL. 95. JUNE, 1923. No. 6.

EDITORIAL

"CONSIDER THE LILIES."

On another page of this issue is an article from the pen of a well-known botanist dealing in a very interesting fashion with the carnivora of the kingdom of plants. This article will be a revelation to those who have never fully appreciated that even in the most demure and refined of nature's families there are members whose codes of living are cruel and not at all in symphony with the codes of the rest of their kindly kindred. For in the family of flowers who would look for aught but pleasing fun in the face of the nodding pansy; who would search for else than winsome charm in the sunlit bloom of the celandine—and who but a lens-toting, net-chasing, goggled academician would ever suspect the happy-go-lucky Jack-in-the-Pulpit of being a pirate of old, cruel and bold, living and thriving on blood and gold. *Arisæma triphyllum* to the high brow, Jack-in-the-Pulpit or Indian turnip to the boy of the country side,—and a fine sort of a preacher is Jack,—standing in Episcopalian rectitude and Presbyterian complacency in a pulpit of many colors, with his sounding board high over his head, and his eye ever staring far into the light of heaven. Jack belongs to a respectable enough family, for even the chaste Lily of Calla, upstanding and proud, only inherits her lovely white form from the same forebears as Jack.

But the pulpit of Jack is only a snare and a delusion. His clerical mien hides an ingrate's ambitions, and many the poor wandering soul coming to Jack for preachment finds only lingering death down at the foot of his pulpit. Jack the Pharisee, unlike his blatant brother, the Sarracenia, is not a true insect-eating monster, but like the Sarracenia he is given to soggy surroundings, and his pulpit is never better built than when it rises in dignity out where the air is humid and the woodlands damp and shady. And so beneath his bowered cathedral arches he holds forth in gay abandon.

To his shrine come congregations of curious gnats and other winged worshippers. The bullfrog and mottled green toad strum their basso notes until the old cathedral hums with holy music; and to the tune of vibrant notes the gnats march on to reverent worship that only ends with heartless sacrifice. On to the slippery pulpit of Jack the winged folks alight, and they no sooner perch on the fatal forum than their little feet slide down the inside walls of the well-greased colored column. Descent into the trap is very easy indeed, but pity the poor creature who tries to climb back. For that is generally such a hopeless task. So the little deluded worshipper finding a return impossible, goes on and on, and down near the base of the pulpit he comes upon a sacrametal ledge where staminate florets exude their fertile pollen. Blundering through these pollen-laden crypts the penitent is swathed in dusty embrace, and on he wanders past into the chamber where the tiny pistillate florets await him to perform his vitalizing penance unaware.

But despite this gracious life-perpetuating act, Jack is still a sycophant, a rank, a gay deceiver, for often our little unsuspecting fly is held a hopeless prisoner. There is no way of escape. Efforts to crawl up the slippery surface are without avail and eventually weak from their constant climbing, the victims, hungry and exhausted, fall prey to the wiles and whims of this arrant murderer of innocent well-doers. Merciful nature sometimes sends her gracious rain to drown the little victims and so reduce their time of pain and stress.

But out in the woodland this is Jack's own month, and the readers will get confirmation of our story of his treachery by opening a few of Jack's pulpits and noting at the base of his malevolent shrine —poor little victims sacrificed heartlessly to the imperfection of Jack's regenerative system.

Thus do we often find in nature the peculiar sacrifice of the higher life to the lower. The cuckoo-pint plants its toxic seed in the body of a living bird, so that the seedlings may find a powerful fertilizer in the decaying flesh into which to strike their rootlets— and the pitcher-plant burns up the death sweat of insects to keep its fires aglowing.

The Master of philosophers who asked his listeners to consider the lilies of the field clinched well his fertile simile, for in the intricacies of a single blossom are lessons enough for all who see aright.

In the beauty of the rose, in the glow of the evening primrose, and in the cannibal tricks of the pitcher-plant, are divergent enough characters to warrant in truth the oft-quoted assertion that man with all his learning can study with profit the sermons in stones and books in humble blossoms.

I. G.

SELECTED EDITORIAL

HAS SCIENCE REACHED ITS LIMIT?

"What is there left for me to discover?" is the common thought of the student as he looks about the library with shelves packed with books or the museum with cases filled with neatly labeled specimens. He realizes that when he enters upon research he is competing not only with his contemporaries, but with all his predecessors. No tariff can protect him from the pauper labor of antiquity.

"What are you scientists going to do when you find out everything about everything?" is a common remark of visitors to a laboratory. The scientist will doubtless reply that life is not long enough to find out everything about anything, but even he is apt to harbor the delusion that all the really big things have now been discovered and that future investigators will find pretty poor picking. Some scientists have been so rash as to put this opinion into print, much to the amusement of later generations. For instance, the great French mineralogist, Hauy, wrote at the beginning of the nineteenth century:

> "Electricity enriched by the labor of so many distinguished physicists seems to have reached a time when the science has no more important steps before it and only leaves to those who cultivate it the hope of confirming the discoveries of their predecessors and of casting a brighter light on the truths revealed."

But we count this the beginning of our knowledge of electricity rather than its end, for over in London at this very time young Michael Faraday in his basement room at the Royal Institution was working out the relationship between electricity and magnetism which has led to the dynamo and the radio.

One might think that such a blunder as this would have made later scientists cautious about thinking that nothing much remained to discover, but, no, for we find in 1894 the catalogue of one of the

largest universities in the United States publishing at the head of its list of courses in physics the following discouraging statement:

> "While it is never safe to affirm that the future of physical science has no marvels in store . . . it seems probable that most of the grand underlying principles have been firmly established and that further advances are to be sought chiefly in the rigorous application of these principles to all the phenomena which come under our notice. . . . An eminent scientist has remarked that the future truths of physical science are to be looked for in the sixth place of decimals."

But the very next year Roentgen discovered the X-rays that led to radium and the electron.

When Newton laid down the law of gravitation the solar system was reduced to a simple mechanism and the movements of the planets could be accurately predicted. What was there left for the astronomer to do? Bigger telescopes would doubtless reveal more satellites and show finer markings on the moon, but how could we ever hope to learn anything about the composition of the heavenly bodies? Yet now we can know how the electrons behave inside the atoms of stars whose light requires thousands of years to reach us, and Einstein has pointed out that even Newton's law requires modification.

Some branches of science may well have reached a terminal. I suppose it is safe to say that about the large animals on the earth have been discovered and described. It is true that the okapi, which is almost as conspicuous as a giraffe, managed to keep himself concealed in the African jungle until 1900, but not many such can have escaped the eye of the zoologist. But he can make no end of queer-looking animals when zoology becomes a constructive instead of a descriptive science.

The scientific discoveries of the twentieth century have not only been more numerous than in any previous century, but they have been greater. Our investigators are not engaged in verifying the sixth decimal, but are projecting far-reaching and fundamental theories.

When you throw wood on a campfire in the night you expand the lighted area, but you also extend the circle of the surrounding darkness. So it is with science. With each increase in enlightenment a larger circle of surrounding ignorance is disclosed.

Dr. E. E. Slosson.

Science Service.

ORIGINAL ARTICLES

ANIMAL-EATING PLANTS.*

Heber W. Youngken, A. M., Ph. M., Ph. D.

Professor of Biology and Pharmacognosy and Director of the Botanical Gardens of the Philadelphia College of Pharmacy and Science.

The great and fundamental rôle of green plants in the world's economy is that of constructing highly complex organic compounds for food out of simple, inorganic, raw materials. This food, part and parcel of their very bodies, is eaten by animals whose chief and contrasting rôle is that of breaking down the plant food into its simplest elements.

The raw materials which constitute the ordinary diet of green plants represent salts of various metals, such as nitrates, phosphates, sulphates, *etc.*, and water which they absorb from the soil, and carbon dioxide, which they inhale from the air during sunlight.

There exist, however, about five hundred species of green plants which have become dissatisfied with the mere common diet of their relatives in the vegetable world and have acquired, in addition, the luxurious appetite for the flesh and blood of animals. These exhibit a variety of devices for the allurement, capture, imprisonment, digestion and absorption of their prey.

Chief among these animal-eating or carnivorous plants are the sundews, fly-traps, pitcher-plants, bladderworts and butterworts. In each it is the leaves which have become modified for the purposes indicated.

The Sundews.

The sundews are curious, small, bog plants that are mainly members of the genus *Drosera,* which comprises eighty-four species, occurring in tropical, warm temperature and cool temperate regions of both hemispheres. Each of these possesses a rosette of leaves that arise from a greatly reduced root system.

The shape of the leaves varies depending upon the species, although it is frequently rotund, spatulate or filiform. The whole upper surface of the leaf-blade is covered with glandular tentacles,

*One of a Series of Popular Lectures, given at the Philadelphia College of Pharmacy and Science.

often of a wine-red color. The glandular heads of these are covered with a viscid secretion that glistens in the sunlight like dewdrops, a phenomenon that accounts for the common name assigned to the members of this group. The tentacles in the central part of the leaf-blade are short and erect and their stalks are green. Toward the margin they become longer and more inclined outward and their stalks are of a wine-red to purple color.

Fig. 1. *Drosera rotundifolia,* a common sundew found in northern peat bogs.

When examined under the microscope, each tentacle shows a slender pedicel terminating in a gland. A conducting bundle containing spiral vessels and simple vascular cells is observed to come off of a fibrovascular bundle in the leaf-blade and run through the center of the pedicel to the gland. Upon entering the gland it is enlarged and spread out into a number of tracheids. These centrally placed tracheids are surrounded by a protective sheath (endodermis), outside of which are two layers of secretory (epidermal) cells with wine-red, granular contents, the outer layer of which is palisade-like. These glands are commonly oval, excepting the extreme marginal ones, which are considerably elongated. They secrete, absorb and are acted upon by various stimulants.

Darwin [1] has shown that when a small object is placed on the tentacles in the center of the leaf these transmit an impulse to the marginal tentacles. The nearer ones first respond and slowly bend toward the center and then those farther away, until finally all become bent over the object. The time essential varies from ten seconds to five or more hours, depending upon the nature, contents and size of the object, upon temperature, and also upon the age of the leaf.

Again, if the glands are repeatedly touched or brushed or if chemical substances are placed on these the marginal tentacles curve inward. The bending part of each tentacle is confined to a limited space near the base. Not only the tentacles but the blade of the leaf becomes much incurved when any strongly exciting substance is placed on the blade.

The time during which the tentacles and blade remain curved over the object varies according to the temperature, character of object, age, *etc.* Doctor Nitschke [2] found that during cold weather both the blades and tentacles re-expand within a shorter period than when the weather is warm. Darwin [3] found that the tentacles remain clasped for a much longer period over objects which yield soluble nitrogenous matter than over those yielding no such matter. After a period varying from one to seven days the tentacles and blade re-expand and are then ready to again respond. It has been shown by the same authority that as soon as the tentacles become inflected over an object yielding soluble nitrogenous matter their glands pour out an increased amount of secretion which becomes acid in nature. These glands, moreover, continue to secrete as long as the tentacles remain closely inflected.

In nature, small insects catch sight of the glittering drops on the tips of the reddish tentacles, and, mistaking these for honey, alight upon the leaf. They become instantly entangled by the viscid glandular secretion. They try to stroke the viscid fluid off of their legs, but only besmear themselves more. Soon they become covered with the sticky substance, which occludes the orifices of their breathing tubes (tracheæ) and they perish in a short time (one-quarter of an hour according to Doctor Nitschke) from suffocation. The surrounding tentacles bend over the insect's body and clasp it on all sides. A digestive juice containing a proteolytic enzyme of peptic character and an acid is now poured out of the glands. This digests the flesh and blood of the insects caught. The water-insoluble

chitinous parts of the body are left on the surface of the blade. If the insect be large, the bending of the tentacles is augmented by the inflexion of the whole surface of the leaf-blade, which assumes a concave shape. With the tentacles also curved over, the whole leaf simulates a closed fist. The glands then absorb the soluble nitrogenous material which is assimilated by the plant.

Among the insects caught by the sundews are gnats, flies, ants, beetles, small butterflies and dragonflies. The last named are captured by the co-operation of two or three adjacent leaves.

Fig. 2. A patch of Venus Fly-Traps growing near Wilmington, North Carolina.

The Fly-Traps.

The fly-traps comprise two species, *viz.*, the Venus Fly-Trap (*Dionæa muscipula*) and the Submerged Dionæa (*Aldrovanda vesiculosa*).

The Venus Fly-Trap is restricted to damp localities of a coastal

plain strip extending for about fifty-five miles north and forty-five miles south of Wilmington, North Carolina, and nowhere over fifteen or twenty miles in width.

Each plant shows a rosette of modified leaves which together are rarely more than six or seven inches across. From the center of these arises a flower stalk bearing a cyme of white flowers which open from April to June.

Each leaf consists of a winged petiole that is studded on both surfaces with small, brown, stellate hairs. The petiole is truncated in front and contracted to the midrib, which suddenly broadens out into a blade composed of two symmetrical halves that can fold together along the line of the contractile and irritable midrib region. Along the margin of each half of the blade are long, stiff, non-irritable bristles, which, on closure of the blade, interlock with each other. On the center of the upper surface of each half of the blade are three spine-like, sensitive hairs disposed as angles of a triangle. Each of these sensitive hairs is composed of elongated cells whose protoplasmic contents show movement. At the base of each is a cylindrical mass of small cells which permits the stiff hair to be bent over. These sensitive hairs are highly irritable and capable of receiving and transmitting a stimulus. Further, over the entire upper surface of the blade are numerous, closely-set, sessile glandular hairs which, after repeated irritation, secrete an acid digestive juice. Each of these, as observed under a microscope in surface view, consists of a rosette-arranged set of cells composed of four to twelve cell radii filled with a crimson-claret pigment.

Each sensitive hair consists of a somewhat elongated structure composed of three parts, *viz.*, base, highly sensitive joint, and insensitive shaft. The base consists of large epidermal cells enclosing a prolongation of mesophyll cells within, that can receive and propagate a stimulus from the sensitive joint to the leaf interior. The joint consists of elongated columnar cells that enclose similar columnar mesophyll cells with soft, elastic walls. The shaft cells are elongated, thick-walled and almost insensitive.

When a stimulus is applied to any sensitive hair, this affects the joint cells and causes upsetting of turgidity and exudation of liquids with a consequent contraction of the elastic cells. The action is propagated to the midrib region where the cells, by contraction along the upper surface and expansion along the lower, cause closure of the halves.

Macfarlane[4] has shown that when an insect alights on a leaf of *Dionæa,* one hair must either be stimulated twice or two hairs on the same leaf at slight intervals apart in order to cause closure. The caught insect produces increased stimulation and a gradual tightening of the lamina occurs under the repeated stimuli until the halves become closely locked. The glandular hairs now pour out an acid digestive secretion which digests the flesh and blood of the insect's body. The soluble nitrogenous substances are then absorbed by the glands and assimilated.

Dr. J. S. Hepburn,[5] of the Constantine Hering Laboratory, Hahnemann Medical College, of Philadelphia, recently found that the secretion of the leaves of *Dionæa* contained a protease which was active in the presence of 0.2 per cent. hydrochloric acid. This enzyme, therefore, resembles pepsin of the gastric juice of man, which also acts in a 0.2 per cent. hydrochloric acid medium.

Dr. J. M. Macfarlane, of the University of Pennsylvania, who with Doctor Canby and Charles Darwin have separately investigated the structure and physiological activities of this plant, reports that two touches one-fourth to one-third of a second apart will not produce closure of the halves, though a second stimulus that is from 1 to 120 seconds apart from the first will effect closure, also that it is not essential for the stimulus to be on one hair, that a prick sets off the trap at once due to liquid escaping from turgid cells, and further, that all muscle stimulants, mineral acids, and ammonia effect closure of the trap.

Among the insects caught by *Dionæa* are earwigs, millipedes, flies, ants, wood-lice and dragonflies. The length of time required for the digestion of their softer parts and the absorption of the soluble products of digestion varies. During this time the trap remains closed. Darwin[6] cites four instances in which leaves after catching insects never reopened but began to wither. Mrs. Treat,[7] who made observations on plants cultivated in New Jersey, noted that "five leaves digested each three flies and closed over the fourth, but died soon after the fourth capture." The power of digestion possssed by *Dionæa,* accordingly, is more limited than that of *Drosera,* which has been known to capture and digest many insects in a shorter period of time.

Aldrovanda vesiculosa, which might well be called a "Submerged *Dionæa,*" is a relative of the Venus Fly-Trap. It is a floating aquatic plant found widely distributed in shallow ditches and

ponds over the old world from Europe to Australia, but nowhere abundant. This plant is entirely devoid of roots, but possesses a slender stem which bears whorls of modified leaves at its nodes. Like the Venus Fly-Trap, each leaf shows differentiation into a winged petiole ending in five narrow processes that connect with a terminal, rounded, incurved blade, divided into equal halves by a sensitive midrib, but the midrib projects beyond the summit of the lamina as a bristle. Long, rigid, spiny bristles extend from the petiole and are thought to prevent the approach of animals unsuitable as prey. The margins of each half of the blade are bent inward and their rims are studded with short conical teeth. Projecting from the upper surface of the midrib and along a line describing the inner third of the upper-blade surface are a number of sensitive hairs and short-stalked, disc-shaped glands, while over the outer portion of the surface are to be noted a number of scattered stellate hairs.

Larvæ of aquatic insects and small species of Crustaceans such as *Cyclops, Daphnia* and *Cypris,* swimming by, occasionally brush against the sensitive hairs and the two halves of the blade close together just as in *Dionœa* and the animals are entrapped. When they attempt to escape through the place where the margins of the blade meet, they find the conical teeth prevent their egress. They die in the trap and when the latter are forced open and examined a couple of weeks later they only contain the chitinous skeleta.

The Pitcher Plants.

The pitcher plants are for the most part found in bogs. Their main representatives belong to the genera *Heliamphora, Sarracenia, Darlingtonia, Nepenthes* and *Cephalotus.* The pitcher itself represents the hollowed-out midrib of the leaf in the first four-named genera and an inpouching of an ordinary leaf in the last-named genus.

Heliamphora[8] is represented by a single species (*H. nutans*), which is only found on and around the base of Mount Roraima, between British Guiana and Venezuela. Here it flourishes in wide-spreading, dense tufts in wet places where the grass is short. It has a rosette of red-veined pitcher-leaves and delicate white flowers raised high on red-tinted stems. Along the entire length of the pitcher are two broad wings. The pitcher itself represents a

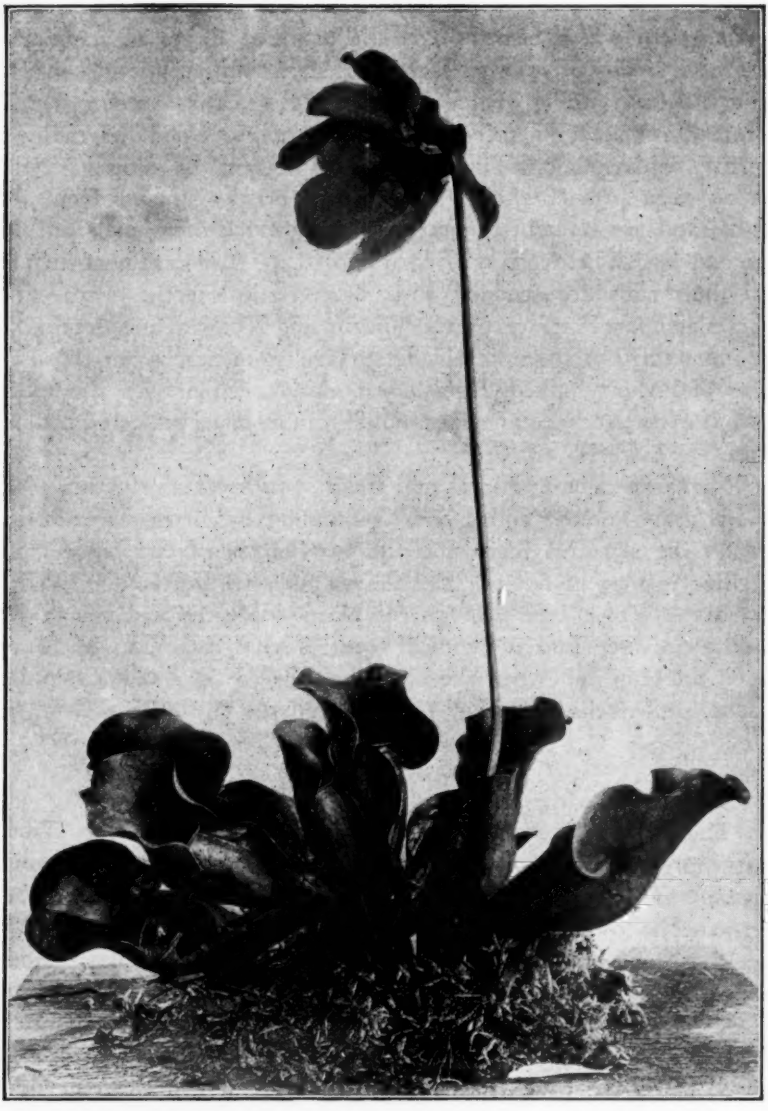

Fig. 3. *Sarracenia purpurea* in bloom. Photographed in Ocean County, New Jersey. This pitcher-plant is our common northern species.

hollowed-out midrib which is tubular in shape, becoming gradually broader from base to mouth and ending in a small lid. Over the entire outside of the leaf are nectar glands and upward-directed hairs. The nectar glands secrete a sweet fluid which entices insects, so that this surface can be termed the alluring surface. Nectar glands also occur on the inner surface of the lid. Next, the upper one-third to one-half of the inner surface of the pitcher is covered with downwardly projecting hairs and nectar glands. This surface can be called the attractive and conducting surface. A smooth surface follows, which in turn is succeeded by a detentive surface in the lower part of the pitcher, composed of mostly smooth-walled cells, a few of which bear short hairs.

Sarracenia[8] is represented by seven species, all of which are confined to Eastern North America except *Sarracenia purpurea,* which extends west to Western Minnesota and West Central Canada. Their pitchered leaves are of varying form and color design, depending upon the species. Frequently they are long-funnel shaped, tubular or vase-shaped. The color of every species varies with its age as well as extent to which it is exposed to bright sunshine. In some respects the form of pitchers resembles *Heliamphora,* but there is only a single wing present and further the lid is considerably larger.

In all we find the pitchers showing an alluring outer surface covered with nectar glands, but devoid of the upwardly directed hairs seen in *Heliamphora,* an attractive inner-lid surface, marked with numerous downwardly directed hairs and nectar glands which lead the insect toward the next or conducting surface. This is either nearly smooth (*S. purpurea*) or it presents delicate, downwardly projecting processes and on which the insect loses its foothold, also (excepting *S. purpurea,* which next shows an intervening glandular zone) a lower detentive zone, in the bottom of the pitcher, which contains a watery fluid and whose surface, save its lowest portion, is marked by the presence of many elongated, downwardly directed, thick-walled hairs, which prevent the ascent of insects that have fallen into this zone from above. Glands are also present on the upper part of the detentive surface.

Darlingtonia[8] is represented by a single species, *Darlingtonia californica,* which grows in mountain swamps and borders of small streams at altitudes of 1000 to 6000 feet from Plumas County in the Sierras of California northward to Jackson and Josephine Coun-

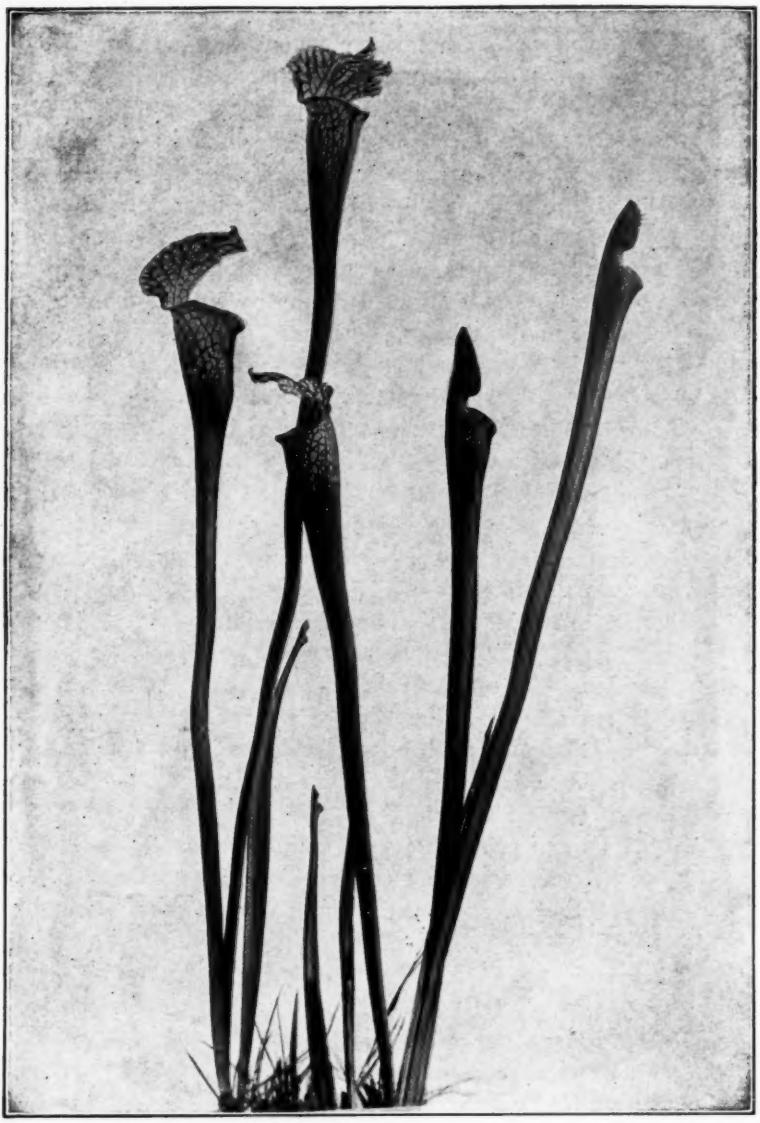

Fig. 4. *Sarracenia drummondii,* a southern species, showing open pitchers and younger pitchers with closed lids and lips. Photographed in Mobile County, Alabama, where the mature pitchers commonly attain a height of 18 to 28 inches.

ties in Oregon. Its underground rhizome gives rise to pitchered leaves which are from one and one-half to nearly three feet in height and spirally twisted in about a half-revolution. Each pitcher expands near the summit into an inflated hood, which exhibits a circular opening up to an inch in diameter on the under side. The

Fig. 5. Darlington's Pitcher-Plant (*Darlingtonia californica*), a western species showing the twisted pitcher and the bilobed flap. Photographed in Plumas County, California, where mature pitchers attain a height of 20 to 30 inches.

dome of the hood is spotted with large, thin, translucent areas. A wing extends along the pitcher from rhizome to its orifice. At the upper and outer edge of the opening is a moustache-shaped append-

age which possesses stiff hairs, all of which point toward the pitcher opening. The color of the pitcher is green, blotched with red and yellow. Within and about the opening and on the bilobed appendage are alluring glands which secrete a nectar attractive to insects. The nectar is also secreted by glands along the wing. An insect creeping over the exterior of the pitcher is enticed to the nectar along the wing, which it follows up to the orifice, where the honey is sweetest. Flying insects are attracted to the pitcher by its mottled and colored features. They alight on one of the flaps of the appendage and follow its curve, which narrows to the orifice. Sharp bristles in the path pointing toward the orifice make it the natural direction for the insect to travel. Upon reaching the end of the path, it is tempted farther by honey glands within the opening of the pitcher, which it next visits. When satisfied and ready to leave, the translucent areas on the hood above, like illuminated windows, entice it away from the opening by which it entered. The insect sees no means of escape, nothing but hairs on the inner surface of the pitcher pointing downward and which direct it to the dark detentive pit below, where it drowns in the watery secretion.

By far the most beautiful and gracefully shaped pitchers are those belonging to the genus *Nepenthes,* which is represented by about sixty-eight species that are mainly indigenous to the East Indies, with headquarters in North Borneo and with Mount Kina Balu as a center. Many of the plants are continuously exposed to a moist, dripping atmosphere.

Each of the modified, pitchered leaves shows a petiole (usually winged) which widens into an expanded blade, the midrib of which is continued as an elongated tendril which expands into a terminal winged pitcher. The pitchers show a large variety of shapes and color designs, depending upon the species. Frequently they are tubular, goblet or cornucopia shaped. Each pitcher has a hinged lid which varies from small elliptic to large heart or kidney-shaped. The tendril is sensitive to contact stimuli and often winds about a limb of a tree. The pitchers, partly filled with a viscid watery secretion, either hang suspended in the air from the tendril or rest on the ground.

One of the largest pitchers found in this group is that of *Nepenthes Rajah,* a species found on Mount Kina Balu along the north coast of Borneo at an altitude of 5000 feet. It has leaves which, exclusive of petioles, are eighteen inches long, and the pitch-

ered portion is six inches in diameter and twelve inches in length, with a circumference of nineteen inches. The lid is ten inches long and eight inches broad. The pitchers rest on the ground in a circle. The color of the pitchers is deep purple. The color of the lid portion is lavender, shading to green at the edges. One pitcher noted by Spenser St. John [9] held four pint bottles.

Fig. 6. *Nepenthes Rajah,* an East Indian species of pitcher-plant.

Nepenthes Edwardsiana, another large pitchered form reported by St. John,[10] is an epiphytic climber found on the north side of Mount Kina Balu at altitudes of 6000 to 8000 feet. One plant measured by this explorer was twenty feet long and had a large cylindrical pitcher on every leaf, twenty-one and one-half inches long and two and one-half inches broad. The base of the pitcher was bright pea-green, the remaining surface a brilliant brick-red. The circular lid was red in the center and green around the margin.

The lower surface of the petiole, lamina and the whole external

surface of the tendril and pitcher are covered with alluring nectar glands. These alluring glands also occur along the stem. Their secretion entices insects to the pitcher mouth or lid. Around the mouths of the pitchers of nearly all of the species is a corrugated rim on which are parallel ridges, which are usually extended as teeth that are inclined downward into the pitcher cavity. The sur-

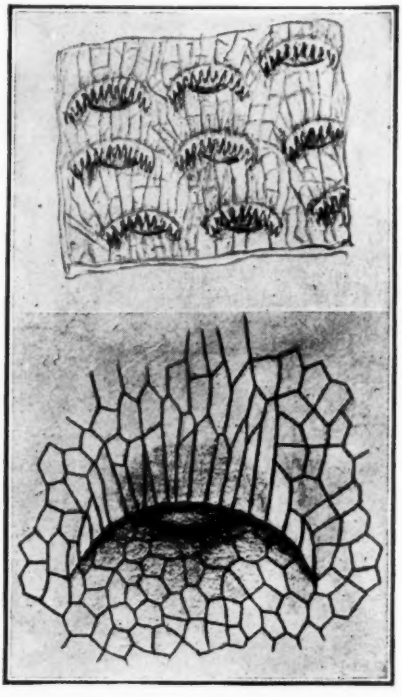

Fig. 7. Digestive glands of *Nepenthes*, each imbedded beneath a projecting flap. A group of the glands is shown in the upper section, a single gland at a higher magnification in the lower section.

face of this rim is smooth and polished, so affording a poor foothold for insects. Around this rim, in the region of the teeth, are the openings of deeply sunken marginal glands which pour forth a very sweet nectar, attractive to insects. The inner surface of the lid is usually dotted with attractive glands.

In many species of *Nepenthes* the entire inner surface of the

pitcher cavity constitutes the detentive surface. It is lined with a smooth epidermis that is uniformly studded with glands which secrete a digestive juice containing a proteolytic ferment and absorb the soluble products of digestion. In many others the upper surface of the cavity is smooth, forming a conducting surface, while the lower one-half or one-third is alone detentive. Insects lose their foothold on the conducting surface and fall into the watery secretion at the bottom of the pitcher.

Cephalotus has but one species, *C. follicularis,* which is native to swamps of South West Australia. It has short creeping rhizomes, which produce annually one set of five foliage leaves and

Fig. 8. *Cephalotus follicularis,* an Australian pitcher-plant.

later a set of pitcher-leaves, which rest on damp soil. The pitchers externally are equipped with winged ridges, which provide a handy means of ascent to the mouth for creeping animals, while their lids are half-closed and mottled with white areas and purple veins and are often mistaken for flowers by high-flying insects. In minute details of structure the pitchers are surprisingly like those of *Sarracenia* and *Nepenthes.* The exterior of the stalk is studded with alluring glands. The margin of the pitcher is corrugated and

inflexed, and all over this area and exterior of corrugation, as well as on the inner lid surface, are an abundance of honey glands (attractive surface). Just inside of the margin is a circular, shelf-like ingrowth consisting of downward-directed cells which resemble the conductive surface of *Sarracenia.* The remainder of the inner surface constitutes the detentive surface.

At the bottom of the pitcher on either side are two beautiful crimson to crimson-claret patches. These have sunk in them huge, many-celled glands which have a fibrovascular bundle terminating in their base. The glands secrete an acid digestive juice which partly dissolves the animal captives. A viscid secretion partly fills the pitcher cavity.

As to relations of the pitchers of these several types of curious plants to animals it may be said that insects, spiders, *etc.,* are attracted to the plants partly by the brilliant colors of their pitchers and partly by the nectar drops exuded by honey glands. They make their way to the exterior of the lid (or appendage in *Darlingtonia*), where the secretion along the outer margin is plentiful. From here they move to the inner surface of the lid and sip the honey. Tempted further by the sight of nectar ahead and often by hairs pointing downward, they step inside the pitcher on to the conducting surface. Upon reaching this surface they waver, slip off and fall into the lower part of the pitcher which is the water holding region. They make numerous attempts to escape, but find exit impossible on account of the downward-projecting hairs. They drown in the liquid and their bodies are either decomposed or digested by a digestive juice secreted by glands lining the lower portion of the pitcher cavity.

The animals caught by these pitcher plants are various. While insects constitute their chief prey, slugs, spiders and rodents have been recorded by observers as having been captured by a number of them. Burbidge[11] observed several *Nepenthes* in North Borneo visited by a small rodent, which, while perched on the margins of the pitchers, bends its head and neck and scoops out the caught insects and devours them. The same writer states that if it attempted such action with *N. bicalcarata,* the two sharp spurs with which the pitcher of this species is provided catch it by the neck and tumble it into the pitcher.

Macfarlane[12] has carefully observed the relations of *Nepenthes* to animals. He states in part that "running insects such as

ants and cockroaches are their principal prey. Cockroaches run up the stem and may pause to sip nectar from the alluring stem glands. Reaching the base of the leaf, they may pass along it, attracted by the presence of honey drops there. They almost invariably run along its under side to shelter themselves from enemies and the hot sun. Moving on restlessly and sipping from nectar glands as they advance, they reach the tendril. The ventral wings and the areas

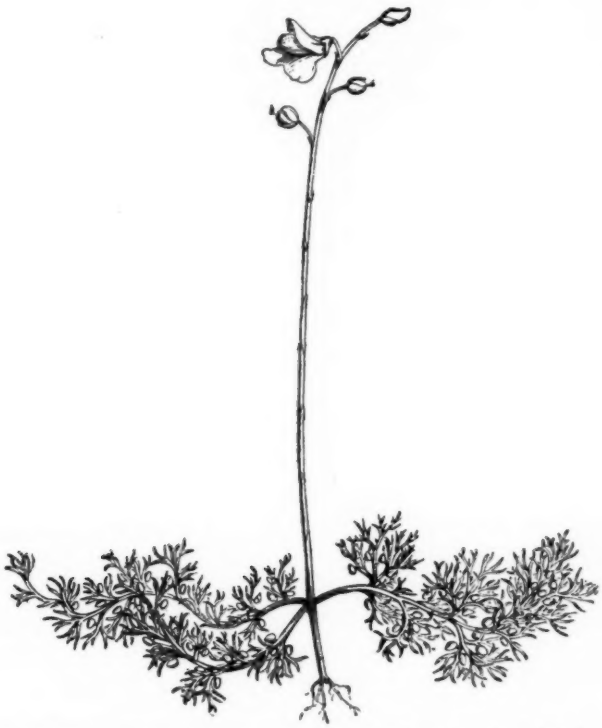

Fig. 9. A flowering plant of *Utricularia vulgaris*, a bladderwort. Note dissected leaves, some of which are modified as bladder-like traps.

between are more beset with alluring glands than is the outer part of the pitcher, and along this they often run till they reach the orifice or lid. The lid glands of the inner surface prove a great attraction, but their secretion does not compare with the marginal glands. Straining to reach the orifices of the glands, the insect

visitors often overreach themselves after a few efforts and tumble into the pitcher cavity, and in rare cases is escape again possible."

Mr. Low, who accompanied Spenser St. John on his travels in North Borneo, found a drowned rat in one of the pitchers of *Nepenthes Rajah*.[9]

The character of the enzymes found in the pitcher secretions has been investigated by Hepburn.[13] This author found a tryptic enzyme in *Nepenthes* which was active in a slightly acid medium. No proteolytic enzyme was found by him in the secretions of *Darlingtonia*, while the *Sarracenias* he investigated were found to possess proteolytic enzymes. The protease in the pitcher liquor of *S. flava* and *S. minor* acts best in 0.2 per cent. hydrochloric acid, while that present in *S. purpurea, S. rubra, S. Sledgei* and *S. Drummondii* acts best in an alkaline solution containing 0.5 per cent. or less of sodium carbonate. Dakin[14] found a protease in the pitcher liquor of *Cephalotus*.

The Bladderworts.

The bladderworts or *Utricularias* are aquatic plants which are found in pools and bogs of various parts of the world, with their centers in South America and the East Indies. The plants are rootless and according to the season of the year sink to the bottom or rise to near the water surface. They have finely dissected submerged leaves, some of which are specialized as bladder-like traps which allow the entrance but not the escape of small animals. Each of the traps represents a greatly modified inflated leaf of vesicular form and usually about one-sixth to one-fifth of an inch in diameter. From the margin of its opening project stiff bristles. There is an upper and lower lip present. The lower lip is greatly thickened and provided with a cushion-like process that extends into the bladder. From the upper lip is suspended a thin elastic valve, the free edge of which rests upon the inner surface of the lower-lip cushion and closes the opening.

Small animals, including crustaceans like *Cyclops* and *Daphnia*, as well as larvæ of small insects and worms, enter the bladders, either because they seek a sheltered harbor for a time from larger prey or because they expect to find food within the bladder. In entering they have to press upon the valve and push it back. As soon as they stop pressing upon the valve, the elastic character of

the valve causes it to close by bringing it back on the under-lip cushion. The entrapped animals struggle to escape by pressing themselves against the valve, but their efforts are in vain, for it is impossible for the prisoners to force the valve outwardly over the cushion, and they die in time either from starvation or suffocation. Their bodies decompose and the water-soluble products of decay are absorbed by quadrifid cells lining the entire inner wall of the bladder.

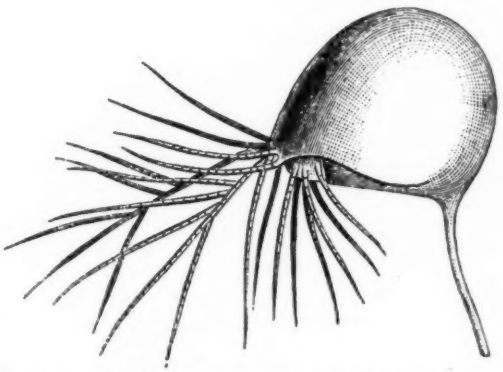

Fig. 10. *Utricularia neglecta.* Enlarged view of bladder-like trap.

The Butterworts.

The butterworts comprise an interesting group of flesh-eating plants which are placed in the genus *Pinguicula.* About forty species exist, of which probably the best-known is *Pinguicula vulgaris,* a member of the *Utriculariaceæ,* which occurs in bogs or other damp places generally in mountainous districts of Northern North America and Europe. Each plant exhibits a root system of from about five to sixteen short, submerged, unbranched roots, from which arises a rosette of oblong-ovate, yellowish-green leaves, the younger central ones being concave and more or less erect, the older marginal ones being flat or convex, with their lower surfaces resting upon the moist ground. From the center of the leaf rosette there arises a slender scape bearing a single flower of violet blue hue that is spurred in its corolla portion.

Alike with other investigated species of *Pinguicula,* the leaves of this plant have somewhat upturned margins, which give them the form of a broad trough, the upper surface of which is covered

with a viscid secretion. Microscopical examination of this surface discloses two types of glands (excepting along the margin), the first being of toadstool shape and consisting of a cylindrical stalk bearing a disc-shaped head of eight to sixteen cells arranged radially, the second consisting of a shorter stalk bearing an eight-celled head.

Darwin [15] and others have experimented with the leaves on living plants of several butterworts and found that drops of water, gum or sugar, and scratching of the surface of these leaves, produced no response, that insoluble solid bodies such as grains of sand and powdered glass allowed to remain for some time caused slight incurving of the margins and a slight increase in the quantity of mucilage by the glands, but that when nitrogenous bodies such as bits of cartilage, meat, clotted blood, *etc.*, are placed near the margin in contact with the glands they are excited and pour forth abundant

Fig. 11. *Pinguicula vulgaris*, a butterwort.

mucilage and an acid secretion. Moreover, prolonged contact with these bodies caused a marked incurving of the margin, which pushed them slowly toward the middle of the leaf, where more glands are present and so increased secretion. This acid secretion completely dissolved these substances, which were later absorbed by the leaf.

An idea of the time necesary for the secretion of fluid and the digestion and absorption of nitrogenous bodies by these leaves may

be gained by the experiment of Darwin with three small cubes of tough cartilage from the leg-bone of a sheep (see *Insectivorous Plants,* by Charles Darwin, p. 382, 1884).

"Within ten hours and thirty minutes some acid secretion was evident, but the cartilage was little or not at all affected; after twenty-four hours the cubes were rounded and considerably reduced in size; after thirty-two hours they were softened to the center and one was liquefied; after forty-eight hours a trace of only one of these was evident and after eighty-two hours all three cubes were liquefied, the secretion was entirely absorbed and the glands were left dry."

When small insects alight from the air upon the leaf of the butterwort they become fastened by the mucilage and in struggling to extricate themselves only become deeper enmeshed by it. Within a short time the acid juice, secreted by the glands as a result of the stimuli, digests their bodies and all excepting their hard, indigestible, outer skeleta (exo-skeleta) is absorbed.

If small creeping insects come upon the margin of the leaf they stimulate the edge to curl over and the marginal glands to secrete. While the insect is enmeshed within the adhesive mucilage, it is slowly pushed by the curling up of the edges into the middle of the leaf, where the acid-secretion glands are most abundant. In about twenty-four hours the softer parts of its body are digested and absorbed and the leaf expands to its normal condition.

Significance of the Carnivorous Habit.

In all of the animal-eating plants which have been investigated structurally and chemically, sufficient evidence has been recorded to warrant the conclusion that these forms have developed their peculiar habit and correlated structure with the object of providing adequately for their nutrition.

Figures 3, 4, 5 and 7 are reprinted by the courtesy of the *Journal of the Franklin Institute* from papers by Hepburn, St. John and Jones.

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EXPLOSIVES AND EXPLOSIONS.*

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To many persons, explosives mean only materials employed in war, but for many years these substances have been of great service in the arts of peace, especially the modern high explosives. Originally, the engineer was the person who operated war engines, which in ancient times were mostly mechanical contrivances for throwing stones or darts. Later, when building, road construction and other public works became the care of trained men, the "civil" engineer was employed. Ancient warfare had some facilities for destructive action by means of fire, and a book that dates from about the eighth century, though probably the original text is older, describes many methods of making burning projectiles. It is entitled "The Book of Fires to burn Enemies," and is said to have been written by "Marcus, the Greek."

The early history of mankind is but little known to us, but we recognize that warfare was soon developed. Our word "toxi-

*Concluding lecture of the Popular Course of 1922-1923 at the Philadelphia College of Pharmacy and Science, delivered May 2, 1923.

cology," derived from a Greek word meaning "bow," refers to that weapon, but especially the poisoned arrow used with it. The display of the rainbow was interpreted by the ancient Jews as evidence that the Deity had ceased warfare against humanity, for he had hung up his bow. The primitive man, who has left no written record, but a considerable amount of pictures and pottery, had very simple weapons, such as the stone, dart, spear, arrow, and, in historic times, at least, the sling-shot and later the more powerful mechanical engines. Of the engines that were employed in the pre-Christian centuries no definite material remains, but some descriptions of ancient writers indicate that stone- and dart-throwing apparatus and the battering-ram were much used. At the siege of Jerusalem by Titus, about 70 A. D., a stone-throwing apparatus of considerable power was employed by the Romans, a stone weighing about a hundred pounds being thrown four hundred yards. The low trajectory and velocity enabled the watchers to see it and they would call out, "Here comes the stone," and the defenders would rush to cover. The Romans painted the stone a dull color to make it less conspicuous, and thus may be said to have inaugurated *camouflage*. Greek fire, that is, the materials described in the book above mentioned, and probably similar materials, were used more or less. Ancient battles, however, were practically noiseless, except for the shouting of combatants.

The date of the invention of gunpowder is uncertain, nor is it clear as to who was the originator. The Chinese appear to have had a gunpowder made essentially as our present product for centuries before Europeans used it. It is known that firearms employing gunpowder were used at the battle of Cressy in 1346, but there are indications of even earlier use. Standard gunpowder is a mixture of potassium nitrate, sulphur and charcoal, but some forms used for mining operations contain sodium nitrate. For many years the standard powder was all that was available for warfare or for blasting. In the earliest use in war, the charge in the gun was ignited by a slow match, later the flintlock was introduced, and finally the percussion cap. The latter method has been perfected so that the material which starts the powder (termed the initiator) is placed in the back of the cartridge, and fired by a piercing needle or some similar device.

The modern high explosives mostly use the oxidizing effect of the nitrates or allied compounds, but differ from gunpowder in

being essentially one compound and not a mixture, although mixtures are often used. The earliest important high explosive of this modern type is guncotton, obtained by immersing common cotton, carefully cleaned and dried, in a mixture of strong sulphuric and nitric acids. The procedure requires care, and by varying the acid strength and other conditions, different grades of explosive can be obtained. Some forms are soluble in a mixture of ether and alcohol. These are rather less explosive and are largely used in the manufacture of collodion. The higher explosive forms can be exploded while somewhat wet, and such a mixture was used a good deal a few years ago. Many other substances analogous to cotton, such as starch, sugar and wood fiber, can be "nitrated" and produce explosives. An important step was made when glycerol was employed. The product "nitroglycerin" is a very high explosive and has found extensive use in engineering operations. It is a liquid, but by mixing it with finely powdered inert material, such as diatomaceous earth or even paper pulp, a safer product is obtained. This is called "dynamite" and is one of the best-known explosives. In later years other substances of this class have come to the front. Picric acid, which is a derivative of the action of nitric acid on phenol, was for many years not regarded as an explosive. It was manufactured for dyers, having the property of dyeing silk and wool a fast, brilliant yellow. An accident that happened in England showed that under certain circumstances it will explode with great violence, and it was used in the Boer war under the name of "Lyddite." It has, however, some acid properties and corrodes the cannon. In the last war, trinitrotoluene, commonly called T. N. T., was used. This is closely analogous to picric acid, but is not acid and, therefore, not so corrosive. Upon the basis on which these few explosives have been produced, many other articles have been made, so that the literature of explosives is now very extensive and in the hands of specialists. Outside of these lines, a number of other very high explosives are known, but they are mostly so uncertain in their action that they have no practical value. By the action of strong ammonia water upon iodin, a brownish-black powder is obtained, which while moist shows but little sensitiveness, but when quite dry will explode violently on the slightest touch. It is obvious that such substances have no practical value.

Explosives have to be adapted to the purposes for which they are used. Two such purposes are especially noticeable. The pro-

jection of a ball or shell involves a somewhat different quality from that of the bursting or rending material. The explosive that throws the shell is not of exactly the same nature as that which bursts it. In recent years another type of chemical has come into extended use, namely, the asphyxiating projectile, but this is not an explosive form and need not be discussed here.

Explosions of great violence may be caused by many substances that are in themselves entirely incapable of such action. Among these are gases and finely divided combustible substances, such as coal, flour, starch and smoke particles. Modern industrial conditions have been seriously complicated by the liability of finely-divided material and the vapors of commonly used liquids to be the cause of severe explosions under comparatively slight influences. Occasionally the violence of the explosion is far beyond what would be expected from the general nature of the material. In some investigations by the Bureau of Mines finely powdered starch was tried, and the explosion was of unprecedented violence. The experimenters, who regarded themselves as at a safe distance, judging by experiments with coal dust, narrowly escaped serious injury. An explosion occurred in a room in which aluminum ware was being polished. The air contained fine aluminum dust and this was ignited (apparently) by an electric spark from a defective connection. Much damage was done. Flour mills have been exploded with complete destruction by accidental ignition of flour dust. In all these cases the effect is due to the admixture of the combustible material with air. Alone, the material burns only slowly at most, and sometimes does not support its own combustion, but mixed with a large volume of air the combustion proceeds with great rapidity, a large volume of highly heated gas is produced and this causes what is termed explosion. The noise of an explosion is probably due to crash of the masses of air that have been separated by the expansion as they return to their original position.

The entire field of explosion and explosives has been very thoroughly studied, not only by scientists solely interested in the nature of the phenomena, but also by the great companies which manufacture explosives, and by the governments that are interested from the point of view of war. In the early part of the late war the Germans made air raids on London, in which much damage was done. For part of the time the material used was "thermit," an industrial product consisting of ferric oxide and aluminum, both in

fine powder and intimately mixed. When ignited, this mixture burns with great heat, but no appreciable explosion. The object of the use of this material was to damage machinery and war apparatus. Thermit is used largely in welding operations. When ignited in contact with the closely approximated parts of a broken shaft, for instance, it promptly and completely welds the two. Therefore, if ignited in contact with any piece of machinery or a cannon, it will so block the parts it touches that they will be useless. It has to be fired by a special igniting mixture. This is, indeed, true of most explosives and highly combustible mixtures, and the study of these "initiators" or "primers" constitutes an important part of the science of this subject.

An interesting experiment may be made by heating ammonium dichromate. This is a crystalline compound having the composition $(NH_4)_2Cr_2O_7$. It is entirely permanent at ordinary temperatures, but when heated it soon produces a flame and liberates gases and a green powder. The products are essentially chromic oxide, nitrogen and water. As water is an easily condensible gas and chromic oxide is a solid, the products do not occupy much space, so that although the substance is of the nature of an explosive, its decomposition is attended by no danger, and by its means we can see what goes on in the closed chamber of a gun when a high explosive is fired. Several substances are known that theoretically may be considered explosives, yet they do not act so under ordinary conditions. Ammonium nitrate, NH_4NO_3, has the composition of an explosive, for it can yield nitrous oxide and water, but when heated gently even in comparatively large masses it decomposes quietly with the production of these substances. Yet it may be that if a proper initiator can be found a more violent decomposition might occur. An example of such an action is noted above in the case of picric acid. A very destructive explosion occurred somewhat over a year ago at the nitrogen-fixation plant at Oppau, Germany. No definite explanation of the accident has been published. It is possible that the German chemists in charge know the details, but if so they have not disclosed them. It is, however, not impossible that they have not been able to determine the cause. The destruction was so extensive and thorough that no evidence may be left to indicate the condition immediately preceding the accident. Some of the high explosives produce effects which cannot be explained on the ordinary principle, namely, that a large volume of gas is suddenly formed.

A few grains of sulphur and potassium chlorate rubbed strongly in a wedgewood mortar will generally produce a loud noise, usually without appreciable action otherwise, but occasionally the mortar will be broken. In such instances, there is no action like the bursting of a shell; the fragments are not projected, and if, as usual, the experimenter is holding the mortar in the hand, no effect is noticed, except a slight stinging. Many other examples of these more eccentric explosives might be given.

Certain forms of guncotton, not as highly explosive as those used in war and blasting, have been long in familiar use. They are more or less dangerous, but rather from their rapid combustibility than from any real explosive qualities. Collars, cuffs and many toilet articles are made from this "low nitrated" cotton, mixed with other substances. The most familiar form is probably the standard motion-picture film. This is inflammable and burns with much vigor, so that such films are not permitted to be shown except under careful protection against fire and panic. The less explosive forms of guncotton are often called "negative cotton," on account of being used in the early days of photography for making the coating on the negative plate in which the sensitive silver salt was held. A solution of this kind of guncotton in ether and alcohol is known as collodion.

Efforts have been made, and are still in active progress, to obtain a film less combustible. At present one form of film is in the market made by means of acetic acid. It is a cellulose acetate, just as the more combustible products are cellulose nitrates. This acetate film is commonly known in the trade as "non-flam," but it is not wholly non-inflammable. It burns very slowly and does not readily maintain its own combustion. It is somewhat weaker than the standard film and this has interfered with its use by the motion-picture industry. It is used in special size in apparatus adapted only to that size for general exhibition, as the insurance authorities do not require a booth or other fire-fighting devices.

The problem of the use of explosives in war has become very serious in recent years because the means of offense are much more effective than means of defense. Submarines and airplanes render armored ships and fortifications of little value. In addition to the ease with which large quantities of high explosives may be thrown on both military establishments and residential districts, poisonous gases are also available. It is thought by many experts that the

next war between any of the great nations will be largely fought in the air. At present there is an enormous development of commercial air service. These machines can be easily and quickly turned into bomb-throwing forms, and the ravages of war extended over the whole of a noncombatant area. Intimately connected with the production of modern high explosives and poisonous gases are the industries based upon coal tar. These have grown up principally in connection with the manufacture of dyestuffs, but the manufacture of most of the high explosives is carried out by an extension of the methods of making what are called the "intermediates," that is, the substances which, though not in themselves colored, produce the colors by being mixed under special conditions. This, which is known as "assembling," is a large part of the work of the dyemaker. Germany for many years was the leader in both the theory and practice of these procedures, and the late war showed how such leadership gave power to the nation that possessed it. Germany is waiting for revenge—Germans, indeed, would not be human if they did not cherish such hope—and it behooves the Allies and Associated Powers who won the war to develop even at some sacrifice a complete system of manufacture both of coal-tar and nitrogen-fixation products.

THE PREPARATION AND PUBLICATION OF RESEARCH PAPERS.

Arthur W. Dox.

A research paper may be defined as a definite contribution to some branch of knowledge, based upon data obtained experimentally. Such data, when accumulated in sufficient amount to warrant conclusions or generalizations not previously formulated, ought by all means to be made accessible to other investigators. To this end, it is customary among scientists to publish their work from time to time in some journal devoted to that particular branch of science to which the work properly belongs. Practically every branch of science has from one to fifty journals, issued periodically, for the purpose of recording recent progress made in its own special field. The authors of the various contributions are the individuals who have conducted the investigations, and the new developments in fact or theory are presented first-hand. Since it thus devolves upon

each investigator to present his own work in a manner acceptable to the editorial staff and to the scientific public, the question of how best to prepare research papers for publication is one that concerns us all.

The preparation of a research paper begins, indeed, before the actual experimental work is undertaken. When we consider the voluminous literature that has accumulated in practically every branch of science, it is no surprise to find that some of our most brilliant ideas have already been worked out by others and published perhaps years ago. Even in the work of our best-known scientists of today the question of priority is occasionally raised. Although the scientific public has little patience with polemical discussions of this nature, nevertheless the scientist who overlooks or ignores some important paper on the problem which he is investigating takes a chance of being called to account. But this, after all, is a small matter in comparison with the waste of time which the unnecessary repetition of another investigator's work entails. Science progresses only as it builds upon the foundation of previous knowledge. The true scientist endeavors to profit by the work of previous investigators and to continue the work where they left off. This does not mean, however, that published data must always be accepted at their face value without a critical examination. Our scientific theories are at best merely tentative, and are useful only so long as they serve as working hypotheses. A critical examination of published literature on any given problem is therefore essential in determining the present status of the problem and in mapping out further work.

It would be a difficult matter to keep track of previous and contemporary investigations on a given problem were it not for the excellent abstract journals which are readily available. By means of these abstract journals it is a comparatively simple matter to prepare a complete bibliography on any given subject. Some of the more specialized branches of science, such as chemistry, botany and bacteriology, have their own abstract journal or "Centralblatt." A careful search through these abstract journals is almost certain to unearth all previous work of any importance on the problem to be investigated. Having prepared a bibliography by the aid of such journals, it is advisable to consult the more important papers in the original. For this purpose a knowledge of German is quite essential, and a reading knowledge of French and Italian is often very

useful. Having thus obtained a general survey of the subject in hand, further experimental work may be planned without fear of unnecessary duplication.

Having prepared the bibliography and subsequently completed the original experimental work on the special problem under investigation, the manner of presentation of the results is of considerable importance. If the paper is to be at all pretentious it is best to divide it into four parts, as follows, each with its own caption:

First.—A brief introduction, stating the problem and the reasons for undertaking its investigation, and its application to the broader field of the special science to which it belongs.

Second.—An historical review, outlining briefly the work of previous investigators, the results they obtained, and finally a statement of the status of the problem at the time the work to be presented was undertaken. Exact citations to the literature should be given, either in footnotes or in a bibliography appended to the end of the paper. This historical review should be preferably chronological in order and critical in style, and the space devoted to each of the previous publications made commensurate with their relative importance.

Third.—The presentation and discussion of the original experiments. This is by far the most important part of the paper and is entitled to considerable detail and amplification. In writing up this part of the discussion it is well to bear in mind the fact that future investigators may have occasion to use the data presented in support of other theories that may be advanced in the light of future work on the problem. It is therefore advisable to describe the experimental work in some detail, including, of course, data that may or may not have an immediate application to the conclusions formulated in the paper. By this it is not meant that conciseness is any less desirable here than in the introduction or historical review. Unnecessary repetition is always to be avoided. The teacher in preparing his first research paper is apt, unconsciously, to make the mistake of applying the well-known methods by which success in that field is achieved. When instruction is imparted by word of mouth a certain amount of repetition is necessary in order to impress the truths upon the listener. You will recall Herbert Spencer's definition of teaching. "Teaching," says Spencer, "is the art of forcing alien truths upon unwilling minds by varied iteration." Rather cynical, to be sure, but quite to the point. On the

other hand, for experimental work which goes on permanent record, repetition is not only superfluous but wearisome. It is an easy matter for the reader to go back and read a sentence or a paragraph the second time if the idea expressed is not grasped immediately. As a matter of fact, however, the editor of the journal generally sees to it that unnecessary repetitions are eliminated. But by having this thought in mind at the outset it is possible to avoid the annoyance of having the article slashed to pieces when it is entrusted to the tender mercies of the editor.

Statistical data should, wherever possible, be presented in tabular form. This enables the reader to see at a glance the scope of the work and to gain a sense of continuity which otherwise is rather difficult of expression. When presenting the paper orally it is, of course, inadvisable to read tables, since these only confuse and weary the listener. But in the permanent record of the work, tables contribute toward the two desiderata, clearness and conciseness. A still more graphic manner of presenting statistical data is the well-known method of plotting curves between two co-ordinates, where the variable may be followed with very little effort on the part of the reader. A discussion of the tables and curves should follow, emphasizing the principal points observed, which furnish the basis for the conclusions to follow.

When well-known methods are used in securing the experimental data, a brief statement and a reference to the paper in which they were first proposed or the modifications suggested is sufficient. New methods, originated by the author, should, on the other hand, be given in sufficient detail to enable future investigators to apply them precisely as used by the author. The one aim to have constantly in mind is the accurate and detailed description of all original work, so that it will be possible for a later investigator, if he deems it expedient, to repeat the experiments without deviation from the original.

Negative results are often quite as valuable as positive results and should usually be recorded. If, however, preliminary trials have been unsuccessful and subsequent work by more approved methods brings the desired results, a simple statement of the difficulties encountered is sufficient. But when the results are uniformly negative, and the author finds that he has, to use a popular expression, been following a false scent, the data are worth recording, if for no other reason than to spare subsequent investigators the waste of

time and the disappointment incident to an unknowing repetition of work which offers little prospect of results.

Fourth.—A formulation of conclusions drawn from the experimental data. This likewise requires considerable care in its treatment. Only such conclusions should be stated as are actually supported by the data secured. Mere speculation or conjecture is entirely out of place. Tentative conclusions are allowable, where the data point to their possible validity but need further corroboration before they can be established beyond question. Such tentative conclusions should of course be qualified, so as to leave opportunity for retraction in case subsequent work of the author or of other investigators fails to bear them out. It is well to number the conclusions consecutively, since this tends toward greater perspicuity. The summary of conclusions is often read by investigators in other fields who have neither the time nor the inclination to wade through a mass of experimental data on topics not germane to their own line of work.

Having now discussed the order of presentation, a few remarks regarding the style of presentation will not be out of place. Scientific treatises have a style of their own, quite distinct from the ornate style of classic literature or of the newspapers of the day. This style would be difficult for anyone but a littérateur to describe, but it may be easily acquired by carefully reading the works of recognized scientific authors. When it is remembered that the object of scientific papers is to present new truths and data in a clear and concise manner, and not to amuse or entertain the public, it is quite evident that anything tending toward the sensational is out of place. It must also be remembered that the scientific paper goes on permanent record. The various journals are bound by the year or by the volume and enter the archives of all the larger libraries, where they are available to students and future investigators. The author may rest assured that when the problem is again taken up for investigation, it may be years hence, his contribution to the subject will be critically read and referred to in the later work. A straightforward style devoid of ornament is best in keeping with the dignity of the science. Rarely does the scientist himself attempt to present his work in a form easily intelligible to the laity. That is usually left to the professional journalist.

As a rule, the scientist is not concerned primarily with the

immediate practical application of his results. Some of the most valuable contributions to science were not fully appreciated or applied on a practical scale during the lifetime of the author. There are of course notable exceptions. But the fact that the work is not promptly received with acclaim is no reflection upon its value and need be no cause of discouragement on the part of the author. The individual investigator is seldom able to prepare a complete monograph on any subject of broad interest, his aim being to furnish a connecting link between the work that has gone before and that which is to follow. Thus it is that the vast fabric of scientific knowledge is built up.

In conclusion, permit me to add a word regarding the compensation the scientist receives for his publications. Very few, if any, of the scientific journals offer the author any financial inducement. Some of the foreign periodicals give a small honorarium, but this seldom more than pays the services of the stenographer in preparing the copy. The scientist may acquire some renown for his researches but others often reap the reward. His work is a labor of love. The intense application required for the successful prosecution of a scientific investigation and the assurance that a definite contribution to knowledge will result, afford an inward satisfaction which cannot be measured in monetary units.

THE FIRST HALF OF THE FIRST CENTURY OF THE PHILADELPHIA COLLEGE OF PHARMACY.*

John Uri Lloyd.

Answered the erudite Dr. Fred Hoffman, pharmacist, author, editor, as in 1890 he sat in the home library of the writer, the subject being an historical review then in process.

"You are safe, Mr. Lloyd, in connection with the personal sketches you have made of those no longer living, but biographical notes concerning persons who are yet with us, regardless of care and fairness, are risky." This comment, by one qualified to make it, often thereafter appealed to the writer of these notes, who at

*A Review of the First Half of "The First Century of the Philadelphia College of Pharmacy, 1821-1921." Published by the Philadelphia College of Pharmacy and Science.

that date was young enough to accept that a line of demarcation could be drawn between the living and the dead.

But in the passing of years, life that is and life that was, are seen by him to coalesce, until in the maturity of thought some may define as the wisdom of experience, one comprehends that whatever service to humanity is accomplished by anyone, never perishes. In that sense the life of an individual passes onward after his face is no longer seen among us. Comes at last a realization of the fact to him who lingers, and comprehends fairly well the lessons taught by Time, the master whose hand fashions each man's past, that—

"He being dead, yet speaketh."

Thus whosoever turns the pages of this testimonial offering to the College of Pharmacy that stands first in American pharmacy annals realizes that the memorable institution as a whole, made up as it is of seemingly separated efforts of self-sacrificing, earnest contributors thereto, who modestly served well their altruistic purpose, is (metaphorically speaking) founded on imperishable, deep-seated granite. Truly the word applies:

"They builded better than they knew."

Pass now resisting thought, if any persons there be inclined to advocate the supremacy of material matter in connection with the "College" now before us. Evanescent to this reviewer's mind is the ponderous building seen with the eye as contrasted with the undying creation uplifted during the years that formed the century that has passed, and which, invisible to eyesight, imperceptible to touch, must indestructibly stand as centuries pass and matter crumbles.

As a closing thought in this direction let us pride ourselves on the fact that not accident but the persistent efforts made by patient men in this College have founded a structure which successors yet unborn, not less energetic, not less enthusiastic, not less serviceable, are destined to amplify as they think onward and build upward.

Since 1821 these several times has the brick and mortar home of the Philadelphia College of Pharmacy been uplifted anew, each building in its day a pride, to become inadequate and then to pass away, giving place to a structure yet more complete. And now, in

its centennial year, the altruistic program of those who heired the responsibilities of the fathers who have gone, bespeaks the early construction of a new College of Pharmacy, second to no building in the world devoted to the problems of pharmaceutical education, practical, theoretical, scientific and professional.

May not this reviewer in connection with the problem as a whole with forecasting thought be pardoned if he indulge in briefly voiced speculation, to the effect that the structure now in contemplation, so complete in all its details, will, if not already replaced, when comes the second century anniversary of the institution be viewed retrospectively as in these lines we touch the edifice erected in the cherished past. Who can doubt that the men and women connected with its upbuilding and those of the future destined to conduct it, clasping hands with those who have preceded, will pass the precious heritage with added laurels to those who are to follow.

True it is that meditations such as these may appear to be out of place with the many who are young and fired by ambition's touch; passably acceptable to those more mature, content in the repose of life's accomplishments; but yet with the few who as companions of this writer linger beyond the allotted age of life they most surely stand unquestioned and undebatable.

But enough. Be this as it may, the duty we have assumed is that of studying the first half of the volume titled *The First Century of the Philadelphia College of Pharmacy, 1821-1921.*

To the alumni of the College one and all, this work must appeal as one of the most precious publications that can rest in the library. This not alone because he finds his name authentically recorded therein in companionship with his classmates, but rather because he can take a just pride in the thought that his very presence and connection with his classmates served in the passing along as an inspiration to the devoted professors of the institution.

May one not imagine with what pleasure each recipient turns the pages carrying the record of the past seeking the names of his classmates as memory appeals? And yet there is a touch of sadness in it all. The pathetic mind touch that comes unbidden when he notes the star before the name of a classmate whose face rises before him under meditation's spell needs no spoken word. And yet, so impartial has been Time with his sickle, that a classmate's recollection of classmates are denied all who precede 1853. The golden star fronts the name of each and every one. Imagine in

this connection what must be the reminiscent thought of Joseph L. Lemberger, 1854, the sole survivor, so far as known, of his own class and all preceding.

Appeal to him as to no other, the portraits and names of the men who taught him and also the preceding professors whom his teachers in their lectures mentioned as having been their instructors. Although none linger other than in name and deed, they speak to him today from the pages of this book. Under memory's spell, comes the familiar voice as when in life the loved professor stood before his youthful face.

Not alone, however, have the classes favored by the opportunity of having been directly graduated from this institution profited therefrom. All in pharmacy are vitally concerned wheresoever they may be situated or whatever may be their present location, be they either directly engaged in pharmacy, or subjects allied with and touching pharmacy.

Whosoever teaches, studies or in business is concerned in pharmacy, finds that the main line, or a branch thereof, radiates from the Philadelphia College of Pharmacy. If anyone ventures to resist the thought probably the party resisting is from pharmacy records afar.

Briefly, one may ask, is there anywhere a member of a college of pharmacy in existence now, or a person holding the diploma of a college sleeping in the past, but with pride recognizes the face of one or more of his teachers among those who sat in the classes of the Philadelphia College of Pharmacy or listened to those instructed therein?

Surely, the greatest pride must come to those concerned in this centennial publication in the fact that throughout the length and breadth of this land the children of this institution have established or inspired what may be called auxiliary colleges which, since 1821, one by one came into being the country throughout.

Thus it is that the printed history of the Philadelphia College of Pharmacy, within the covers held in the hand of the reviewer, speaks but a fraction of what it might voice if there could be added thereto a record of the services rendered pharmacy as a whole by the graduates therefrom who elsewhere serve their Alma Mater.

Nor is this all. Take the record that lies in the outside, beyond the direct sphere of the graduates. Dovetails not this into the

knowledge gained by teachers and students who were never so fortunate as to personally sit in the classes? What do persons even in lands afar owe to literature emanating from this institution? For ten decades the contribution has as a whole been a world's instructor. If credit be given to whom credit is due it is apparent that the pages printed in behalf of pharmacy research, application, and history, as shown in the published records of the American Pharmaceutical Association, THE AMERICAN JOURNAL OF PHARMACY, every journal on pharmacy past and present, every American book written on the subject of pharmacy, in fact all that touches pharmacy in print past or present, is directly or indirectly connected with the men whose lives were spent in founding this celebrated college.

In retrospective thought do we not owe a duty to those who speak not now in words but live in deeds? Before the founding of this institution, pharmacy was taught in Philadelphia by men who instructed the first president as well as officers of the College before us, but which they were not destined to behold. Did not Christopher Marshall, the apothecary, druggist, botanist and chemist, educate and guide Charles Marshall, who in 1821 became the first president of the Philadelphia College of Pharmacy? Were they not perhaps the very first to manufacture chemicals in young America? Note their portraits, pages 28 and 29. Did not Charles Ellis, Dillwyn Parrish, Frederick Brown, receive their earliest instruction in pharmacy in the drug establishment of Charles Marshall? Turn to page 24. Consider John Morgan, the pharmacist-physician, first teacher of theory and practice of medicine, materia medica, pharmacy and pharmaceutical chemistry, in America, whose history was so admirably written by our late friend Dr. M. I. Wilbert, whose pleasant face is pictured on page 203.

Pass next into the record of medicinal chemicals. What a monument of service is the history of the men whose names stand today so prominently before the world as America's earliest manufacturers of medicinal chemicals. How can one separate their deeds, their offerings to the world, from the Philadelphia College of Pharmacy, or from Philadelphia itself? Note plate, page 34, which carries the faces of Thomas H. Powers, George D. Rosengarten, William Weightman and John Farr, the predecessors of the famous establishments of Powers and Weightman, and Rosengarten and Sons, in themselves a world inspiration.

Who can separate the links that connect the manufacturers of

technical chemicals, embracing such names as Samuel Wetherill and the other Wetherills of white-lead fame; Carter and Scattergood, manufacturers of bichromate and prussiate of potash, and other heavy chemicals so necessary to a nation's progress, from the College of Pharmacy of Philadelphia? Imagine their pioneering problems such as bringing white-lead ore in wagons from Tennessee and West Virginia to be smelted in Philadelphia, as accomplished by the Wetherills in the beginning of the last century.

But enough. To attempt to even mention the names of the men who did well their work in connection with and making possible the Philadelphia College of Pharmacy would require a volume.

Even Benjamin Franklin was vitally connected therewith, for did he not, after the organization of the Philadelphia Medical Society, which united with the American Philosophical Society of Philadelphia, print in 1734 the first medical book in covers in Philadelphia, titled "The Poor Planter's Physician, Every man his own Doctor"?

Consider the names of the authors in botany and allied sciences, standardized now as having spoken the first word in American pharmacy and medicine. Let us mention Dr. Cadwallader Golden, Dr. Thomas Cadwallader, John Bartram, Dr. John Redmond. In this connection, *The Botanists of Philadelphia and Their Work* (by Harshberger), a publication of 457 pages, should be consulted.

Dovetailed in it all come the names of men whose special preparations in pharmacy stand yet familiar today. For example, Frederick Brown, the originator of Brown's Jamaica Ginger; Charles Ellis, the fourth president of the Philadelphia College of Pharmacy; Daniel B. Smith, scientific scholar and teacher, collaborator with Wood and Bache in the preparation of the United States Dispensatory, one of the founders of the College and for twenty-five years its president, as well as the first president of the American Pharmaceutical Association (1852); Elias Durand, the French botanist-pharmacist, who in connection with Doctor Tongo translated Edwards and Vavasseur's *Manuel de Matiere Medicale;* Dillwyn Parrish, fifth president of the College; Augustine J. L. Duhamel, celebrated for scientific research; William Procter, of whom it has been said, page 403, "The American Pharmaceutical Association was the offspring of Procter's able and versatile mind," and also that he was the father of American pharmacy; Edward Parrish, brother of Dillwyn Parrish, aforementioned, professor of theory and practice of pharmacy, author of the textbook, *Introduction*

of Practical Pharmacy, later called *Treatise on Pharmacy.* Appeals deeply this book to this reviewer.*

It is as yesterday that came the telegram from Fort Sill, Indian Territory, which informed the friends of Professor Parrish that while on an exploration journey he had died in the then-distant West.

Again, fearing that the space at our command is more than filled, and imagining that the reader has long since cried "Enough!" yet as we live in the past and continue to turn the pages and read the lines, face after face rises before us. For example:

Should we neglect the names of William R. Warner, the first manufacturer of sugar-coated pills in America; Dr. Robert Bridges, the assistant of Professor Bache; Robert Shoemaker, pioneer manufacturer of medicines, developer of machine-made plasters and man of affairs of Philadelphia generally; George D. Coggeshall, who, a graduate of the College, was afterward active in the organization of the New York College of Pharmacy; George W. Kennedy, so conspicuous for years in the American Pharmaceutical Association; Israel J. Graham, early exponent of the process of percolation, and others equally serviceable whose names unmentioned here have been recorded.

These, and such as these, in the opinion of this writer constitute the imperishable foundation of the Philadelphia College of Pharmacy. On this never-to-be-destroyed foundation, whilst civilization such as we now comprehend, lives, stands the edifice of today. To this it may be added, that, not less energetic, not less sacrificing, not less earnest, have been and are the men and women who constitute the actors in the second part of the century that has passed. The record of their deeds, however, will be the pleasurable duty of him who continues this review.

And now it may be asked, have we sustained the assertion made in the introductory passages of this review to the effect that not brick and mortar, not material things visible, but the imponderable essence of life's activities as shown in the united efforts of sacrificing men in times gone by constitute today the Philadelphia College of Pharmacy, and that the founders "builded better than they knew"?

*This book (1864 edition) together with "Fowne's Chemistry," of the same year, "Comstock's Chemistry" of prior date founded the Lloyd Library, as textbooks of the writer of this article. They are yet on its shelves inscribed at the dates mentioned.

ABSTRACTED AND REPRINTED ARTICLES

THE STATUS OF INSULIN.*

In November, 1920, while reading an article by Barron, on the relation of the islands of Langerhans to diabetes, F. G. Banting, then assistant in physiology of Western University, London, Ontario, conceived the idea of preparing an active extract of the islet tissue. Barron had called attention to the fact that degenerative changes occur in the acini of the pancreas following ligation of the ducts, and it occurred to Banting that therefore, after sufficient time had elapsed, the pancreas could be removed and the islet extract elaborated. It had been known that total removal of the pancreas in dogs results in severe and violent diabetes. However, attempts at feeding pancreatic tissue had been without beneficial results, and injections of various extracts of pancreatic tissue, although securing a reduction in sugar, had been followed by symptoms which did not warrant their use in the treatment of diabetes. In fact, a complete review of the available literature warranted Banting in formulating an opinion (1) that the secretion produced by the acinous tissue of the pancreas is in no way connected with carbohydrate utilization; (2) that all injections of whole gland extract have been futile as a therapeutic measure, and (3) that the islands of Langerhans are essential in the control of carbohydrate metabolism. It seemed clear, therefore, that the relation of the pancreas to carbohydrate metabolism was dependent on some process controlled by the islet tissue, and Macleod suggested two possible mechanisms whereby this control might be exerted: (1) The blood might be modified while passing through the islet tissue, and (2) the islets might produce an internal secretion.

The First Experiment.

In May, 1921, the feasibility of the experiment having been recognized by Prof. J. J. R. Macleod, work was begun under the latter's direction in the Physiological Laboratory of the University

*Reprinted from *Jour. Amer. Med. Assoc.*

of Toronto. Under suitable anesthesia, dogs were depancreatized by appropriate surgical methods. Other dogs had been operated on and the pancreatic ducts ligated. After suitable time, the latter dogs were given a lethal dose of chloroform, the degenerated pancreas swiftly removed and then an extract prepared. This extract was injected intravenously into depancreatized animals. As a result, it was shown that intravenous injections of such a solution invariably exercised a reducing influence on the percentage of sugar in the blood and the amount of sugar excreted in the urine. The extent and duration of the reduction varied directly with the amount of the extract injected, and the presence of the extract enabled the diabetic animal to retain a greater percentage of injected sugar than it would otherwise. At that time it was the opinion of Drs. Banting and Best that boiling of the extract made it impossible for it to have an effect on the reduction of blood sugar, and that preparation of the extract in neutral saline solution with retention under cold storage conditions would permit the extract to remain active for seven days. This, in brief, is an account of the first experiments on the production of insulin. This account does not, however, give any indication of the scientific methods employed, of the thoroughly accurate check on the work through the use of suitable controls, or of the great significance of the final result. Furthermore, it says but little of the many years of research by hundreds of physiologists all over the world who contributed their mite to the knowledge of this subject and who trembled repeatedly on the threshold of the final discovery without carrying their experiments to the logical conclusion. It remained for Banting, as the result of an accidental observation made while casually reading an article outside the field to which he devoted himself, to see the final step.

The experiments first carried out by Banting and Best justified the conclusion that some constituent of the pancreas destroys the active principle of the internal secretion of the gland when extracts are made of the whole gland substance by the usual methods. It therefore became apparent that some method of inhibiting this destruction must be secured in a method for preparing the active extract, and for producing it on a larger and more satisfactory scale. Previous experiments by other investigators gave ground for the belief that the pancreas of the fetus furnishes to the mother an internal secretion which is necessary for the metabolism of sugar. This suggested to the Canadian investigators that fetal pancreas

might prove a source of an extract rich in internal secretion, and yet free from the destructive enzymes of pancreatic juice. Experiments were therefore performed, utilizing extracts of fetal calf pancreas, and the results of these experiments showed that neutral saline extracts prepared from the pancreas of the bovine fetus at about the fifth month, when injected intravenously and subcutaneously in depancreatized dogs, markedly reduce the percentage of blood sugar and the daily urinary excretion of sugar. With such injections, a depancreatized dog lived for seventy days. It had previously been shown by Allen that completely diabetic dogs did not live more than fourteen days.

Preparation of the Purified Extract.

In view of the results thus far achieved, the assistance of J. B. Collip of the Department of Pathological Chemistry in the University of Toronto was secured, to take up the problem of isolating the active principle, and with his collaboration an extract was prepared from the whole gland, sterile and highly potent, which was suitable for administration subcutaneously to human beings. With the assistance of Drs. W. A. Campbell and A. A. Fletcher of the Department of Medicine in the University of Toronto, its use was undertaken on patients with diabetes in the wards of the Toronto General Hospital between December, 1921, and March, 1922. The effects of the preparations were observed in seven cases of diabetes mellitus, and it was shown that the results observed in animals could be paralleled in man. Following the injection of the extract, there is a rise in the respiratory quotient indicating carbohydrate utilization, and also a return to the normal blood sugar level. Furthermore, the patients reported a complete relief fom the subjective symptoms of the disease. The results warranted the conclusion that in these extracts "we have a therapeutic measure of unquestionable value in the treatment of certain phases of the disease in man." However, it was also found that, without careful control, severe toxic reactions may be encountered, and the authors warn that this will undoubtedly be a factor in the evaluation of the ultimate therapeutic utility of the method. In the meantime, Professor Collip had shown that an active extract could be prepared from the pancreas of the full-grown ox by using alcohol as an extracting medium so as to circumvent the destructive action of trypsin, as was previ-

ously shown by E. L. Scott. The fact that the extracts first studied seemed to cause a certain degree of irritation and involved the use of pancreas of special character and available only in small amounts caused Dr. Collip to elaborate a method for preparation of the extract from adult pancreas by fractional precipitation with alcohol. Briefly stated, it was as follows:

"The best method for separating the active principle from protein, salts and lipoids was found to be the following: Equal volumes of fresh minced pancreas and 95 per cent. alcohol were allowed to stand for several hours with occasional shaking, and then filtered. To the filtrate was added 2 volumes of 95 per cent. alcohol. After allowing several hours for precipitation of most of the protein, filtration was repeated, and this filtrate was evaporated to small volume in vacuo at a temperature of from 10 to 30 C. An aqueous extract was thus obtained, which was washed twice with ether in a separatory funnel to remove lipoids, and then further distilled in vacuo to a pasty consistency. Addition of 70 per cent. alcohol and centrifugation then resulted in the formation of four layers, namely, a bottom layer of salt crystals, above it a saturated aqueous solution of salt, above this a flocculent layer of protein, and on top a clear layer of alcohol containing the entire active principle in solution. This top layer was pipetted off, and delivered into several volumes of 95 per cent. or (preferably) absolute alcohol. Several hours were then allowed for the active principle to precipitate out. It was then dissolved in distilled water, concentrated by vacuum distillation, filtered through porcelain, tested for sterility, and delivered to the clinic. Such extracts, practically free from proteins, salts and alcohol-soluble substances, could be made isotonic and injected subcutaneously without local reactions."

During the preparation it is necessary to keep the acidity of the fluid correctly adjusted.

Dosage and Assay.

It now remains to devise a method for securing accurate dosage, and it was determined that the effect of an extract might be measured by its results when injected into rabbits. Large doses of insulin cause hyperexcitability, followed by coma, rapid breathing, sluggish reflexes and dilated pupils. The effects, on the whole, resemble those of strychnin poisoning. Slight stimuli, even shaking of the floor, caused violent convulsions lasting one or two minutes, and death finally resulted from respiratory failure. Coincident with the appearance of these symptoms is a lowering of the blood

sugar. After a large number of these experiments, it was found satisfactory to consider as one unit the amount of insulin which, on subcutaneous injection, can lower the percentage of blood sugar to 0.045 within four hours in a rabbit, weighing about two kilograms, from which food has been withheld for from sixteen to twenty-four hours. Recently prepared solutions are concentrated so that a small volume may contain a sufficient number of units. As pointed out by Macleod, the reason why 0.045 was chosen as a percentage to which the sugar should become lowered is that at this level, almost without fail, the animal develops highly characteristic symptoms. As indicated later, this method of assay is not wholly satisfactory and efforts to arrive at still more accurate standards are being continued.

In the meantime, the investigators continued to study the effects of the extract on the chemistry of the blood and the urine in the establishing of a number of important points. It was shown that in the presence of insulin the power to metabolize carbohydrates is restored. When insulin is given, the acetone bodies entirely disappear from the urine, and remain absent so long as the administration is maintained. It is shown that insulin, possibly because of its primary influence on carbohydrate metabolism, also effects the metabolism of fat.

It has been known that a number of procedures will produce hyperglycemia and glycosuria, among them puncture of the floor of the fourth ventricle of the medulla, subcutaneous injections of epinephrin, and the various forms of asphyxia, including ether anesthesia. It was then shown that in rabbits previously fed abundantly with carbohydrates so as to insure a high percentage of glycogen in the liver, none of these experimental procedures would cause more than a slight increase in the blood sugar in animals previously injected with insulin. The importance of the remedy in surgical operations under ether anesthesia in diabetes can therefore be estimated.

As pointed out by Macleod, the therapeutic effects of insulin in diabetes mellitus in man were definitely forecast by animal experimentation in each instance. After all of these effects had been determined in the laboratory, the drug was administered in hospital wards. Had administration been permitted unguided by the results of these observations on rabbits, it seems almost certain that sooner or later an overdose would have been given, causing convulsions,

and there would have been no indication as to what remedy should be used. But the experiments on rabbits showed clearly that these serious symptoms may be immediately antidoted by injection of glucose. Furthermore, in several patients in whom these symptoms have appeared, injection of glucose has immediately and permanently removed them. Finally, January 6, 1923, Drs. Banting, Campbell and Fletcher published in the *British Medical Journal* the results of the administration of the drug in fifty cases. The most striking results have been seen in children and young adults, and it is stated that all the patients were benefited by the treatment. On the first and second days of treatment, if sufficient insulin is given, the urine becomes sugar-free, and on the second or third day ketone-free. The patient becomes conscious of increasing strength before the end of the first week. Hunger is replaced by appetite, thirst is lessened, edema disappears in about ten days, and considerable amount of physical vigor is restored. The weight frequently increases, and this can be brought about by supplying food in excess of the caloric requirements and with it an increased amount of insulin. One patient, aged sixteen, who had lost forty pounds (eighteen kilograms) during three years of diabetes, gained thirty-five pounds (sixteen kilograms) in less than four months.

The Distribution of Insulin.

As pointed out in the journal January 6, 1923, the discoverers of insulin have assigned their rights in the product to a committee of the University of Toronto, and patents have been applied for in Canada, the United States, Great Britain and other countries. The committee has decided to expand the production of the drug by collaborating with some firm regularly engaged in the manufacture of organ extracts. A firm was secured which undertook, under an agreement with the university, to manufacture the product. By this agreement, the university contracted not to issue licenses to other firms in the United States until the lapse of a period during which the large-scale method could be carried out so as to yield the output of a preparation of standard and uniform potency, both when assayed by the rabbit test and when tested therapeutically on diabetic patients. The firm agreed "to distribute a sufficient number of free samples of their preparation to various physicians specializing in the treatment of diabetes in properly controlled clinics." This

collaboration has been in effect for several months, and the American manufacturer has submitted his product to the Council on Pharmacy and Chemistry, which will, no doubt, issue a report within the near future. A product is also in course of submission from the Canadian manufacturer who co-operates with the Toronto insulin committee.

Source of Insulin.

One of the problems that is giving most concern to the investigators has been the provision at a reasonable price of a considerable quantity of the extract. The entire animal kingdom has been investigated, and particular attention has been given by Macleod to the proportion of potent insulin products from the pancreas of certain fishes. These fishes have been particularly investigated, because in them the islet tissues are separated fairly definitely from the remainder of the pancreas. These experiments are continuing, but it is not possible as yet to state definitely whether or not this will constitute an important source of the product.

Mode of Action of Insulin.

Other investigations have been concerned largely with the mechanism by which insulin produces its satisfactory results. Thus, Forrest, Smith and Winter have shown that insulin and liver extract *in vitro* cause an alteration of the rotary powers of glucose and fructose without a corresponding alteration of the copper-reducing power. They state that "a possible explanation of the action of insulin is that it causes a shifting of the equilibrium in the direction of increased -glucose formation, which is stored or utilized, and that the increased utilization of sugar by the diabetic after the injection of insulin may be put down to the increased formation of this type of glucose." Their experiments seemed to show that a continual supply of insulin is necessary for the working of some enzymatic body which is responsible for lowering the blood sugar, for the blood sugar invariably rose between insulin injections.

Carrying out the experiments on rabbits still further, McCormick, Macleod, Noble and O'Brien have shown that there is an immediate decline in blood sugar during the half-hour following an injection of insulin, but a variability both in the time of onset and in the rate of recovery which afterward occurs. The

rate of the initial fall is independent of the nutritional condition of the animal. After from thirty to ninety minutes, the blood sugar rises more rapidly in glycogen-rich animals than in those glycogen-free. Within wide limits the dose of insulin has no constant influence on the rate of the fall. These observers have been unable to find that insulin has any influence on the rate of glycolysis in sterile, incubated, defibrinated or oxalate blood, or in mixtures of blood and expressed muscle juice. They have elaborated the view that sugar must disappear from the blood because it passes into the tissues, that insulin no doubt also passes out of the blood into the tissues, and that when it enters the tissue cells it sets up in them some process that leads to the immediate disappearance of sugar as such, so that a "vacuum" for sugar is created in the cell, and sugar is withdrawn from the blood more rapidly than the supply can be replenished. "It is possible," the authors say, "that the first step in this process is the formation of some compound between sugar and insulin, and that this may occur in part in the blood itself; but it is unlikely that such an intravascular process is any essential step in the disappearance in blood sugar." In view of the fact that the blood sugar rises much more rapidly in glycogen-rich animals than in those which are glycogen-free after the initial fall after the injection of insulin, the authors consider that it is impossible to make a precise physiologic assay of insulin by determining the percentage of blood sugar at varying periods following its injection. The approximate assay may best be arrived at by measuring the blood sugar from ninety minutes to three hours following the injection in animals from which food has been withheld for twenty-four hours. When considerable doses of insulin are given, the typical toxic symptoms may not appear until the percentage of sugar has fallen considerably below the level of 0.045, at which they most frequently occur with weaker doses. It is therefore the final conclusion that the occurrence of these typical convulsions cannot be depended on as an exclusive method of physiologic assay.

Clinical Use of Insulin.

From the fifty cases originally studied by Banting and his collaborators, and from a large number of cases studied by the investigators in various American diabetic clinics, a number of facts relating to the clinical administration of insulin have been determined.

In view of the great potency of the remedy for harm when improperly used, it is wise to begin at once to emphasize these facts and to impress them repeatedly on physicians in order that permanent harm may not result. The picture of a successful result has already been given. Such a result is secured when a correct dosage is administered to a patient who, at the same time, is receiving a properly selected diet. Early in the work, preparations of insulin contained certain amounts of protein and split protein products. The natural result was a toxic reaction in a certain number of cases. The present products are practically protein-free, so that with the exception of urticarial eruptions in one or two sensitive patients such reactions were not observed among the fifty patients first studied. However, the fall in blood sugar, as has been mentioned, may produce a characteristic train of symptoms when the blood sugar falls to 0.07 per cent. Under the influence of insulin, the patient becomes promptly aware of this. He may first complain of hunger or, most often, of a sense of weakness or fatigue; and, especially if it is his first reaction, he is conscious of some anxiety or of what he calls nervousness, or he may even show signs of a definite neurosis, with a loss of emotional control, such as crying spells. Almost constantly present is a feeling of tremulousness; but actual tremor is rarely seen. The patient may also have some inco-ordination of finer movements. Vaso-motor phenomena, such as pallor or flushing, a sense of heat, of chilliness or a profuse sweat are common. Should the hypoglycemia increase and the lowering of the blood sugar come to 0.05 per cent., there is an acute distress or mental disturbance, such as confusion and disorientation. Finally, a blood sugar of 0.032 in one patient resulted in a state of coma with hypotonia and loss of the deep reflexes. Several of the patients suffered difficulties of articulation when the blood sugar reached the lower levels mentioned.

Fortunately, these serious symptoms may be relieved by the immediate administration of food. From fifty to one hundred cubic centimers of orange juice has an almost immediate effect in clearing up the symptoms. A better result is obtained with from five to twenty-five grams of glucose given with orange or lemon juice. "When a patient is unconscious," says Banting, "one cubic centimeter of epinephrin (1:1000 solution) should be given intramuscularly, followed by glucose by mouth, and if the patient is not well enough in a few minutes to swallow glucose, it may be given

subcutaneously or intravenously." Special nursing precautions should be adopted for detection of reactions when insulin treatment is first started, when a new preparation is given and when insulin is administered late in the day, as the reaction may occur during sleep. The patients soon recognize the state of a reaction, and may be able to avert the symptoms of their own accord.

In view of the fact that the insulin effect on the blood sugar is not exerted immediately after subcutaneous injection, it is customary to space the injections so that their effect occurs during the period of assimilation of carbohydrates. This means that the insulin is injected at, or shortly before, the meal. But instances occur, possibly due to delayed or too rapid absorption of sugar into the blood stream, or the use of diets containing too much carbohydrate in which glycosuria may occur or which a reaction may follow. To Banting, this emphasizes the necessity for observing diabetic patients for a short time in the hospital under insulin before returning them to their homes for general treatment.

In establishing the insulin treatment, it is advisable to begin with a moderate dose, gradually increasing it until the desired effect is obtained. The amount of insulin used will depend not only on the carbohydrate tolerance of the patient but also on the height and fixity of the blood-sugar level. At present the authors believe that the best results are secured by aiming at maintaining a normal blood-sugar level. This is accomplished by injecting insulin in relation to a meal at which a certain amount of carbohydrates is given. As the patients improve, the amount of carbohydrate is increased, and at the same time the amount of insulin is increased.

The most important uses of the product are unquestionably in juvenile diabetics, in whom the mortality previous to the introduction of insulin was almost 100 per cent., diabetics who are undergoing surgical operations, and diabetics with coincident infections, such as tuberculosis, gangrene or syphilis. Many diabetics at the present time are able to exist comfortably and satisfactorily with a well-selected diet. On the other hand, many diabetics are not thus amenable to treatment. In the latter group of patients, under the proper administration of insulin, glycosuria was abolished and ketones disappeared from the urine and the blood, the blood sugar was markedly reduced and maintained at normal levels, the alkali reserve and alveolar carbon dioxid of patients in acidosis and coma returned to normal, the respiratory quotient showed evidence of

increased utilization of carbohydrates, and the cardinal symptoms were relieved with marked clinical improvement. In diabetic coma, insulin may be characterized as a specific.

Conclusion.

It appears, then, that as a result of a vast amount of research on diabetes mellitus, and still earlier on the physiology and pathology of the pancreas, researches by numerous investigators all over the world, conducted largely on experimental animals, as well as with human beings, there has finally been evolved from the pancreas a principle which has a specific effect on the carbohydrate metabolism of the body. The effects of this extract have been thoroughly studied, and its limitations rather clearly defined. A method of assay is being perfected, so that it appears likely that the product will shortly be made generally available to the medical profession. Improperly used, results may occur of such seriousness as to interfere greatly with establishing the true worth of the product. To secure proper results, a knowledge of scientific dietetics is necessary, and carefully controlled laboratory observations are important. Physicians who plan to use the remedy must inform themselves fully of its potency, the symptoms of danger, the proper methods of administration, the proper methods of antidoting unfavorable effects, and the correct manner of evaluating results. If these precautions are observed, there seems to be no reason why any well-trained physician should not be able to use the remedy satisfactorily.

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SCIENTIFIC AND TECHNICAL ABSTRACTS

THE ASSAY OF ETHYL CHLORIDE.—Richaud (*J. Pharm. Chim.*, [7], 1923, *27*, 329) presents a review of the processes given in the more important pharmacopeias for the assay of this substance. The main principle involved is that as ethyl chloride does not ionize promptly in water, any hydrochloric acid or other ionizable impurity will be detected by the addition of silver nitrate. It is probable that action of water for some time will bring about a limited hydrolysis, by which ethyl hydroxide and hydrochloric acid will be formed, hence the rule that the precipitate must not appear promptly. Richaud considers the direction of the French Codex as ambiguous, as it may be understood either as requiring a test of the sample mixed with water and then another portion mixed with cold alcohol, or as requiring the use of a water solution of silver nitrate and then a second test with an alcoholic solution of the same reagent. It is not necessary to discuss the problem thus raised, but the review of

the methods in other pharmacopeias and the description of some of his own experiments will be interesting.

If a drop of alcohol (90 per cent.) is added to a few cubic centimeters of cold ethyl chloride, a turbidity occurs, but the addition of more alcohol clears the liquid. Richaud regards this transitory turbidity as due to the dehydration of the alcohol, the separated water appearing in a finely divided form. The further addition of alcohol corrects the insolubility and the water disappears. To test this theory, absolute alcohol was added to the chloride. No turbidity was produced. Moreover, the turbidity noted above can be removed by addition of water and shaking the cooled mixture. Even the addition of an excess of silver nitrate solution will clear the liquid. The slight turbidity that may be observed in testing ethyl chloride with silver nitrate is not due to a reaction of the silver with the chlorine ion, but to the separation of water. Of course, this statement applies only to pure samples.

The majority of pharmacopeias direct the test to be made not on the sample itself but upon the solution obtained by shaking a portion of the sample with water. The U. S. P. (IX) alone directs the test upon a mixture of ester with alcohol, but it gives the amount of alcohol to be used.

The French Codex of 1908 rubric is "Ethyl chloride in aqueous or cold alcoholic solution should not give immediately a precipitate with silver nitrate."

The Br. Ph. (1914) states that two volumes of the ester are to be shaken with one volume of water, and the separated water should not redden litmus nor give a precipitate with silver nitrate. Further, if sulphuric acid is shaken with ten times its volume of the ester, the acid separated and diluted with an equal volume of water should be odorless and give no turbidity with silver nitrate.

The Swiss Ph. presents a more complicated method. The vapor of the ester is passed through water, and this is tested with litmus paper which should not be reddened. Nitric acid and silver nitrate are added. No precipitate should appear.

The U. S. P. has already been noted. Richaud regards the amount of alcohol directed as much too great. Four or five volumes will be sufficient.

The Belgian Ph. uses the Swiss method of passing the vapors

of the ester into water, and requires that this solution should not redden litmus nor react with silver nitrate.

The Japanese Ph. gives: "Agitate 5 cc. of the sample with an equal volume of water previous cooled to 0° C. The separated water should not redden litmus nor give a precipitate with silver nitrate after addition of a drop of nitric acid."

The German Ph. gives: "Five cc. of ethyl chloride are shaken with five cc. of water which has been cooled in ice. The separated water should not redden litmus nor give a precipitate with a drop of silver nitrate."

Richaud's conclusion from his experiments and comparison of other pharmacopeias is that the Codex should be amended so as to provide for the addition of the silver nitrate solution to the ester previously diluted with several volumes of alcohol.

H. L.

PREPARATION OF STARCH JELLY FOR TESTING AMYLOLYTIC ENZYMS.—The susceptibility of catalysts to interference renders great care necessary in making investigations as to their actions. The starch-transforming catalysts are especially subject to interfering conditions, and different starches differ much in their susceptibility to the actions of diastase and the pancreatic enzym. Arrowroot starch is one of the most easily hydrolyzed. In a recent issue of *J. Pharm. Chim.* ([7], 1923, 27, 333) Astruc and Renaud present the results of many experiments with especial reference to the French Codex method of assaying pancreatin. They find that, among other matters, the screening of the starch should be uniform. They recommend a particular size of screen, but the unit is not given in absolute dimensions. The starch sample should be prepared in some quantity, its response to a standardized pancreatine noted and small portions kept in ground-stoppered bottles in the dark. A limit of moisture content (say 7-8 per cent.) should be fixed, and the jelly that is being hydrolyzed should be agitated constantly. Potato starch is recommended in the French Codex. The authors suggest certain modifications of the rubric, but these do not concern American pharmacists.

H. L.

STUDIES IN ALCOHOLIC FERMENTATION.—Notwithstanding the ban which is now on the manufacture and sale of intoxicating beverages and the low alcoholic percentage which has been fixed as the limit, the fermentation industries are too important commercially and too interesting scientifically to be neglected either by the research or technical chemist. The production of alcohol from sugars goes back to a remote past. It appears that so far as that part of the world in which the earliest written history remains, the production of wine, the fermented juice of the grape, was the initial procedure. The operation requires but little skill, although refinements of taste and the influence of external conditions give rise to special products. The grape carries on its skin the yeast cells necessary to fermentation, and the fairly definite acidity of the juice controls the fermentation. Pasteur was the pioneer in this field, and recognized the importance of the acid condition, but it has only been of late years that the influence of hydrogen-ion concentration in biologic action has given a better understanding as to the *optimum* condition of the yeast enzyms. In the fermentation of cereal grains this control of acidity is not so definite, hence brewing requires a more careful supervision than wine-making. Yet it is an interesting fact that the members of the great Nordic race which withstood the Roman power were essentially drinkers of malt liquors, while the Romans used wine. The two peoples also differed in the source of their fat diet, for the inhabitants of the Mediterranean basin used olive oil largely, while the fat of milk was an important item in the diet of the other race. Many years ago a writer of a history of botany pointed out that the men of the olive and vine lands found themselves checked in their victorious career by the men of the beer and butter land. Whether the high vitamin content of butter as compared with vegetable oils had any part in determining superior fighting power cannot be ascertained.

The chemistry of the fermentation of the hexoses has been generally considered as comparatively simple. A simple breaking up of the sugar molecule into two molecules of carbon dioxide and two of alcohol has always been given as the reaction. It has been long known that in ordinary fermentations accessory substances, such as aldehyde, glycerol and some esters, are produced in small amount, but these were often ascribed to the action of species of yeast other than those constituting the greater portion of the mass. For

some time, however, brewers have been using pure cultures, and this explanation does not apply. The production of glycerol was not regarded as of any industrial importance, but during the war Germany's lack of fats brought about a scarcity of glycerol, and German chemists succeeded in developing methods of fermenting sugar so as to secure a much greater yield of this substance than was formerly noted.

The mechanism of hexose fermentation has been made the subject of extended investigation by Carl Neuberg, who presented a summary of his results last September at the centennial celebration of the German Society of Naturalists and Physicians, at Leipzig. The communication was in the form of a lecture and is given in full in the *Berichte* (1922, *55*, 3624). A comprehensive summary of it is given by René Fabre in *Ann. Chim. Pharm.* [7], 1923, *27*, 298. The data given in the present article are taken from the French text, but the German original has also been consulted.

The simple reaction shown in our textbooks is due to Gay Lussac, but it merely shows the end-point of the principal change. Today we know that most of the decompositions of complex molecules are accomplished by stages, many of which are often so quickly passed that it has been impossible to detect them definitely. The whole range of catalytic actions is probably of this type. Under the influence of invertase, sucrose is converted into dextrose and levulose. The reaction can be represented by a simple equation showing the sucrose molecule assuming a molecule of water and the group breaking up into a molecule of each of the hexoses. This, however, is merely a statement of final result. It has been assumed that one intermediate stage is the union of the invertase with a limited amount of sucrose molecules, the taking of the equivalent number of water molecules, with subsequent re-arrangement of this association, by which the hexoses are formed and the invertase released. This, again, is but a statement of principal actions and involves unproved views.

In 1910, Buchner, at a meeting of the French Chemical Society, gave a summary of the views then generally accepted. The suggestion of Von Baeyer that lactic acid is an intermediary in the fermentation of sugar was not generally accepted. Buchner suggested the formation of some substance prior to that of lactic acid, such as dioxyacetone, and Boysen-Jensen succeeded in demonstrating the formation of this in the alcoholic fermentation of dextrose.

These, and similar views, not appearing to be satisfactory, Neuberg took up the matter and made an extended investigation. In 1910 he discovered that pyruvic (pyroracemic) acid, $HC_3H_3O_3$, is rapidly converted under the influence of yeast at room temperature into acetaldehyde and carbon dioxide. This action is due to a catalase, that Neuberg termed carboxylase. This is found associated with a catalase termed by Neuberg "sucrase," which is probably the one that causes the splitting of the hexose. It is also found in many other fungi. Carboxylase is able to resist a temperature that injures the other enzym, and it is stated that the two may be separated by dialysis. Sucrase and carboxylase affect other substances than pyruvic arid, especially the higher homologues thereof, with a result corresponding to that with pyruvic acid, namely, the production of carbon dioxide and an aldehyde of carbon content corresponding to the acid treated. These higher aldehydes may, however, undergo further transformations. Carboxylase, Neuberg found, is also to a certain extent a proteolytic enzym; at least it can act on amino-acids. It becomes then of much interest and importance in biologic chemistry. Other investigators found similar enzyms in bacteria and mushrooms.

From the investigations of Neuberg and others it seems probable that intermediate between the hexoses and the formation of carbon dioxide and alcohol, there appears a compound containing three atoms of carbon, pyruvic acid. In 1913, Neuberg and Kerb suggested a series of reactions in the fermentation of dextrose, by which methylglyoxal, glycerol, pyruvic acid, acetaldehyde and alcohol were formed through different lines of decomposition. The methylglyoxal is produced by removal of two molecules of water from a molecule of dextrose; the glycerol and pyruvic acid by hydrolysis of dextrose, the acetaldehyde by the removal of one molecule of carbon dioxide from pyruvic acid. Ethyl alcohol is formed by the simultaneous hydrolysis of methlyglyoxal and acetaldehyde, the oxygen of the hydrolyzing molecule going to the methylglyoxal and the hydrogen to the acetaldehyde.

The intricate chemistry of these processes is set forth in the article, but enough has been given to show how re-investigation of chemical actions which are generally considered as entirely solved will yield data that are both novel and interesting.

H. L.

MEDICAL AND PHARMACEUTICAL NOTES

DEARTH OF QUININE IN THE NEAR EAST.—There are no manufacturers of perfume and toilet articles in Turkey, according to the American Chamber of Commerce for the Levant, which calls attention to the fact that the import trade in this line is very important, Constantinople importing annually perfumes, face powders, toilet soap, shaving cream, dental preparations, face cream, brilliantine and rouge in large quantities.

At the present time this trade is largely divided among France, Germany and England. Cheap perfume is practically controlled by Germany. The principal trade of English firms is in toilet soap; trade in brilliantine, face cream and rouge is largely monopolized by France.

Such drug and drug-store specialties as antitoxins, serums, surgical supplies and sundries would find a big market in Western Greece, according to Consul George R. Stiles, of Patras, who calls attention to the fact that this kind of commerce has been little exploited by American producers, although the 2,000,000 inhabitants of the western mainland, and especially the rich provinces of the Peloponnesus, are estimated to import annually over $1,000,000 worth of these articles. The few American reminders found in this market are said to have been well received.

While the American trade experts dilate on the opportunities for American imports of drug and druggist sundries in the Levant, there are thousands of people is the Caucasus who are actually dying in large numbers for want of American quinine. The national headquarters of the Near East Relief has received word from the director of relief operations in the Caucasus that there is no limit to the amount of quinine that would be used to advantage because of the great scourge of malaria. Quantities of army medical supplies were donated by the United States Government to the Near East Relief last year, but these are about exhausted, and unless American drug firms respond to the present emergency inhabitants of Armenia, Adjaristan, Dagestan and Azerbaidjan are threatened with extinction. Between five hundred and one thousand pounds are needed to meet the present crisis. Many people are unable to support them-

selves because they have become utterly exhausted by malaria, thus creating a very serious relief problem. Under-nourishment reduces the natural resistance of the body to the inroads of this disease.

Since the vitality of the natives is so lowered, it has been impossible for American relief to find enough able-bodied men to carry out the large drainage systems and sanitation projects necessary to cope with the conditions that produce a malarial scourge.

UTILIZATION OF WILD MILKWEEDS.—The common milkweed, *Asclepias Syriaca L.*, is one of the most abundant weeds of the Eastern United States. It blooms towards the latter part of the summer, bearing a large number of flowers gathered in close bunches, and having a slight but agreeable flavor. Few pods develop, but each of these contains about a hundred seeds, each bearing a long tuft of silky hairs. The plant contains in its leaves and stalks an abundant latex of the nature of rubber, but there is no likelihood of any commercial value in this. The seed-hairs seem also to be without value as textile material. It appears, however, that the seeds yield a valuable oil, and a recent number of the *Bull. d. Mat. Gras.* of Marseilles states that experiments have shown that the oil is a drying one and will serve for paints. One hundred kilos of seeds will yield about twenty-two kilos of oil, but it is thought that by improved methods of cultivation a greater yield may be obtained. The oil is not suitable for use alone as a drying oil, but in admixture in moderate quantity with linseed oil, a good-drying oil with much elasticity is produced. It can also be used in varnish. The refuse seeds are not suitable for cattle feed, as they contain a poisonous principle, but have some fertilizing value. *Asclepias tuberosa L.*, which is a more ornamental plant, also is oil-bearing. The flowers of species of *Asclepias* are complicated and require the visits of insects to bring about fertilization, which probably accounts for the fact that a bunch of several dozen flowers often yields only two or three pods. It would probably be of advantage, therefore, if *Asclepias* plantations should be established to have bee-hives nearby.

H. L.

SOLID EXTRACTS

A new preparation to prevent dimming of windshields on automobiles, or glass windows at sea has been adopted by the Navy Department after long research on the subject by the Chemical Warfare Service. It avoids the use of castor oil which was the base of similar preparations used during the war.

The new substance is a sodium salt of sulphonated rapeseed oil, with an excess of caustic soda, and a small amount of water glass, glycerine, and engine oil. It may be applied in sticks or by wiping the glass with a cloth impregnated with it.

A windshield so treated remained clear after having been driven through a dense fog for thirty minutes. Tried at sea it was found effective against fog, rain, and spray, although it was necessary to renew it after each rain. Preliminary tests on submarine periscopes have been so satisfactory that 150 sticks were made and will be distributed to the submarines for further tests.

Iusulin, or "isletin," the new diabetic remedy, is still scarce despite the fact that it seems to be widely distributed in nature. Animal pancreatic glands yielded the original product which the Toronto experimenters discovered but now the scientists tell us that it may be prepared from yeast, from fish scales and glands, from onion tops and sprouted grain and from many other sources. Hail the day when its production will be so multiplied that the poor sufferer as well as the rich diabetic may share in its blessings.

"The purer the ether the better the anæsthesia." Since the days of Long and Morton that was the dictum of pharmacology. But now, after 75 years of blind belief, it is announced absolute diethyl ether (pure "sulphuric ether") while a grim narcotic poison is not a desirable surgical anæsthetic.

The ethers routinely used for surgical anæsthesia owe their anæsthetic properties to the presence of certain synergistic gases—thus a new era in anæsthesia.

The Chemical Warfare Service of the U. S. Army is experimenting with a "sneeze gas," which may be mixed with illuminating gas so as to save lives by warning room occupants of the escape of gas. Over in London another serving scientist nullifies the efforts of our army chemists by blatantly announcing the discovery of a non-poisonous illuminating gas, which can be commercially produced at a cost below that of the present manufactured gas. And it is also claimed that it is the equal of manufactured gas in thermal units.

Contrary to a general impression, fats are easily digested foods, according to a recent investigation made by Dr. C. F. Langworthy of the U. S. Department of Agriculture. There is little difference in the digestibility of animal and vegetable fats, he states, nor is there any difference due to the flavor if properly prepared. Cod-liver oil is one of the easiest digested.

Androdedotoxin, the poisonous principle contained in the leaves of the rhododendron, has been studied pharmacologically by Dr. S. W. Hardikar, of the University of Edinburgh. This substance when administered in large doses causes death by paralysis of the heart muscle, while in smaller amounts its fatal action is due to the failure of breathing through its action on the nerves to the muscles of the chest which are concerned in the act of breathing, this investigator states.

A few years ago it was noticed that sheep in the neighborhood of Edinburgh showed toxic symptoms after eating rhododendron leaves, with fatal results in some cases. Interest in such observations led Dr. Hardikar to study the poisonous substance which these leaves contained.

Traces of impurities are often necessary for the successful promotion of many chemical processes, occasionally, however, these impurities are detrimental to the process. For instance, in making dry batteries, traces of iron in the pyrolusite or of copper in the ammonium chloride are highly objectionable. One part of sulphur per million in cocoanut oil is said to create trouble in the soap-making process. In lead burning traces of arsenic in the hydrogen used to make it impossible to secure a good joint. Attempts to make a good nickel-steel were for years frustrated by impurities present in the commercial nickel of the day.

The resurrection fern of our Southern States, a plant which remains in a state of suspended animation during drought, has been known to survive for more than a year without water.

A novel scheme for determining the velocity of the blood stream and noting its variations from the normal rate in the several prime diseases is accomplished by injecting a stain into one arm while the blood is dripping from the corresponding vein in the other arm. Every five seconds the escaping blood is examined for the first appearance of the stain. The interval in healthy men was found to be 20.7 seconds, and in healthy women 20.8. A delay in the appearance of the stain in the other arm is an early sign of incipient insufficiency of the circulation.

The gland tidings have reached the ears of fish and fowl fanciers. The gold fish raiser feeds his infant fan tails on desiccated thymus glands and piscatorial prodigies result. By feeding brown leghorn chickens dried thyroid glands, the appearance of normal plumage is delayed in the chicks and fowls with feathers of different form and color of those fed on ordinary diet are said to be produced.